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Vol. 19 MARCH, 1946 No. 3

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 19 MARCH, 1946 No. 3

Original Communications

PREOPERATIVE DIETARY MANAGEMENT FOR SURGICAL PATIENTS

WITH SPECIAL REFERENCE TO LESIONS OF THE STOMACH AND DUODENUM

RICHARD L. VARCO, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

FOREWORD AND INTRODUCTION

IN THE past a surgeon matured by focusing his attention upon, and acquiring a broad familiarity with, pathologic tissues and a facility with operative techniques. Such achievements appeared paramount because so many technical developments in surgery antedated a commensurate knowledge of physiologic processes, or application of this knowledge, when it was present. A transition is being effected. One of the most laudable changes in recent decades has been the steady reduction in the number of "emergency operations." The emphasis on speed and manual dexterity has been supplanted by a more leisurely technique stressing precision and a genuine respect for tissues that yields generous dividends in improved wound healing and decreased postoperative reaction. In addition, the surgical viewpoint is being altered by a shift in emphasis during the years of graduate training from a background of anatomy and pathology exclusively to one including an orientation in the biologic sciences. Merely fortuitous circumstances have not brought about this transition, but it has resulted rather from the wise guidance of those teachers recognizing the advantages ultimately so accruing to the earnest student of surgery. A broad knowledge of fundamental physiologic processes enhances the capacity for recognition of pathologic deviations, frequently arouses a curiosity as to the mechanisms involved, and often suggests appropriate therapeutic principles. Maintenance of this familiarity with the biologic sciences and their application to phenomena encountered in clinical material is the sort of correlative thinking certain to keep surgery dynamic and of ever-increasing

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usefulness to all of mankind. The lower mortality rates (and shortened morbidity) of this era eventuate from many factors, for today's doctor is not only a better operator, but he takes better care of his patients and is, therefore, a better surgeon. At least partial solution of the problems of hydration, electrolyte balance, hemodynamics in shock, intestinal obstruction, and nutrition, among others, are responsible for this improved management of surgical cases.

In all these fields progress has been disproportionately advanced compared with the accomplishments in the dietary care of surgical patients. And, whereas a host of investigators have been concerned with these other complex tasks, a rather small group has dealt with nutritional care. This universal widespread lack of inquisitiveness is unfortunate since more frequently than seems to be appreciated, patients, ill with diseases remediable by surgery, present mild to severe states of starvation or malnutrition. A condition of marginal nutritional imbalance, it appears, may be present in an individual for a prolonged period before the onset of another illness, either of a secondary or unrelated nature. The bodily requirements are thereby augmented above the patient's limited intake, thus making the real need acutely manifest for the first time. There is a broad zone existing between optimal nutrition and classical deficiency states in which abide many borderline cases of unsatisfactory dietary management and/or inadequate food intake. Alertness is necessary, therefore, to detect not only those cases in which the patients are subsisting on manifestly deficient diets but also the instances of occult inanition. During such semi- or starvation states, in both man and animals, survival is at the expense of bodily substance. Man has the capacity to exist in this autocannibalistic predicament for prolonged periods deriving his caloric needs partially or wholly from his own tissues. During this interval, though sustained, he suffers from the compound evils of a diet low in protein content and with the majority of its calories derived from fat. If prolonged, this utilization of a high fat diet, low in calories, simulating as it does so closely experimental conditions in animals, evokes detectable evidence of hepatic dysfunction and hypoproteinemia. Clinical experience has shown that particularly in such cases in man, extensive, prolonged surgical manipulations are poorly tolerated, and occasionally such individuals react unfavorably to relatively minor procedures. They exhibit an instability of blood pressure, dis proportionate to any actual hemorrhage during the operation, which responds unsatisfactorily, often, even to transfusions of blood and plasma. During the convalescence the vitality seeps steadily away despite the employment of a variety of therapeutic measures, and, whereas, the pathologist may seem to offer exoneration with the finding of bronchopneumonia or beginning heart failure, in reality the issue was unfavorably settled when the decision was made to operate upon an ill-nourished individual. The fatty liver and hepatic dysfunction developing in such instances and responsible, at least in part, for such tragedies are problems whose significance and remedy are unquestionably of great surgical importance.

Cases 1 and 2 are appended to illustrate just these points and are fairly typical recordings of the tragic sequence of events in patients who have suf-

fered a large recent weight loss and then had a major operation without adequate provision for nutritional rehabilitation.

CASE 1 (No. 703974).—S. D., aged 47 years, was operated upon elsewhere for an incarcerated ventral hernia which was reduced and repaired; but one month after returning home, a second operation was performed by the local doctor to relieve a recurrent intestinal obstruction. Recovery was slow and incomplete, so that the patient still had signs,

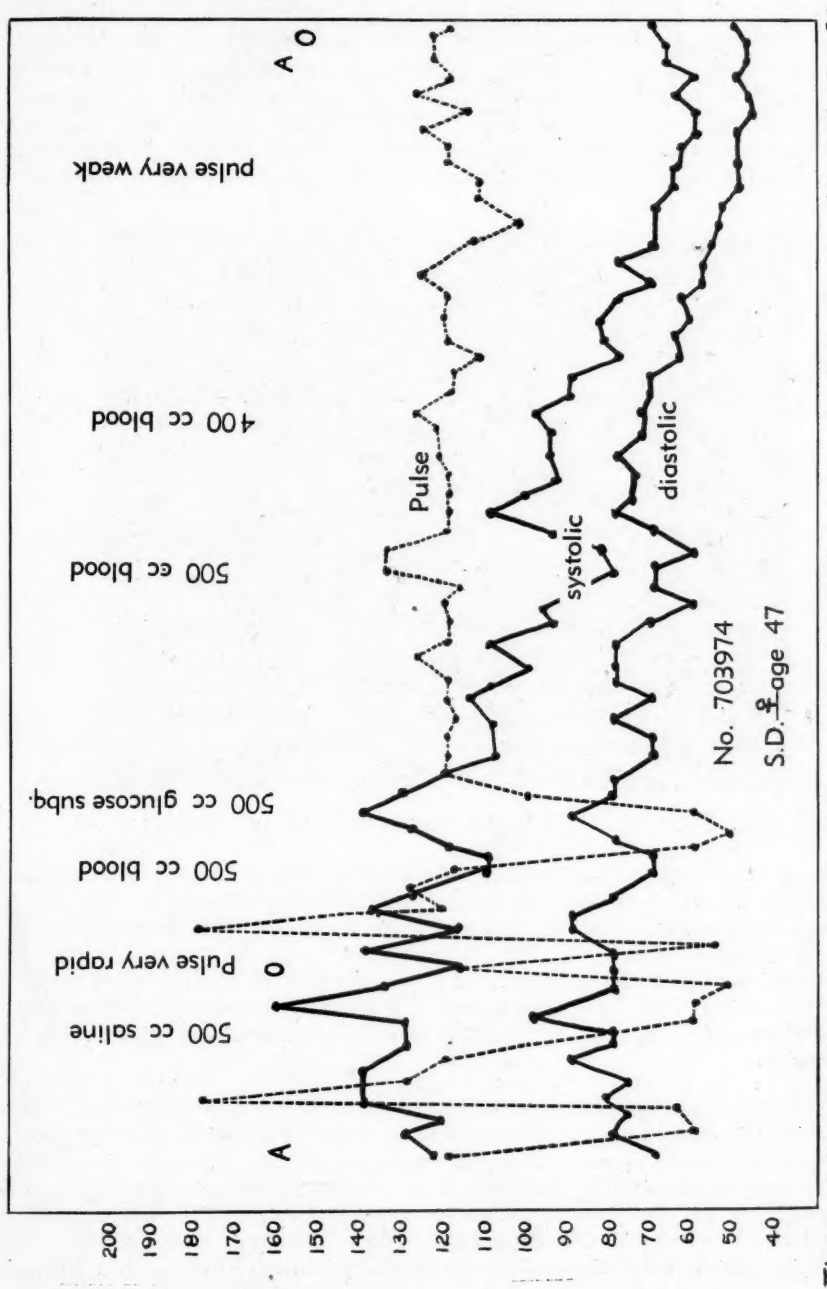


Fig. 1.—Record of blood pressure, pulse, and intravenous fluids during anesthesia (Case 1).

and was suffering from attacks, of intestinal obstruction at the time of her transfer to this hospital. During this interval the patient had lost much weight and had been eating irregularly and in small amounts. Soon after admission, physical symptoms and signs plus x-ray findings of acute small bowel obstruction, of the incomplete and nonstrangulating variety, were present. This condition was treated with intestinal siphonage maintained about two weeks and until shortly before surgery. Whereas electrolyte, fluid, and hemoglobin values were controlled by the appropriate intravenous and subcutaneous therapy, little attention was accorded the protein and caloric requirements. The patient lost an additional 5.4 kilograms after admission and prior to surgery. At the time of operation a partial enterectomy and colectomy were performed to remove the sites of obstruction. During this procedure wide fluctuations in the blood pressure and pulse were noted. The blood pressure was unstable, out of all proportion to the actual blood loss. There was a steady reduction in pulse pressure as can be noted in Fig. 1, despite liberal transfusions with blood and plasma during the operation. In the immediate days postoperative the

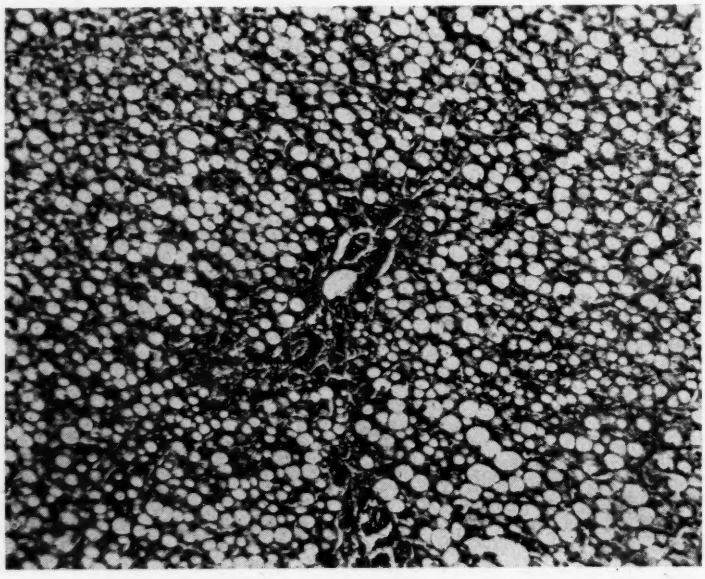


Fig. 2.—Photomicrograph of a section from the liver (Case 1).

pulse rate remained high and the blood pressure exhibited a great lability and a distressing tendency to fall to shock levels. The patient deteriorated steadily and died eleven days later with a temperature of 108° F. The pathologic report was: (1) hepatic insufficiency with marked fatty metamorphosis of the liver (marked degree of this change reproduced in the photomicrograph shown in Fig. 2), (2) jaundice on basis of liver damage, (3) congestive heart failure, (4) pulmonary edema, (5) bilateral hydrothorax and ascites, (6) cloudy swelling of kidneys, and (7) evidence of recent abdominal operation on small and large intestine.

Case 2 (No. 711332).—E. P., aged 71 years, had, in the five months prior to admission, noticed epigastric distress and fullness, occasional bouts of vomiting, and increasing fatigability, and a fifty-pound weight loss, representing 33 per cent of her total body avoirdupois. The x-ray diagnosis was carcinoma of the stomach. She received plasma, amino acids, and glucose for four days in a quantity sufficient to yield about 1,000 calories and was given also a full liquid diet by mouth. Some of the latter was removed by daily gastric aspiration. A subtotal gastric resection was performed after the four days prep-

aration had restored electrolytes, hydration, and hemoglobin to normal values. During the operation, and persistently afterward, as shown in Fig. 3, the blood pressure displayed a tendency to fall, the pulse was consistently rapid, and the pulse pressure was reduced. These conditions prevailed despite generous repeated transfusions of blood and plasma

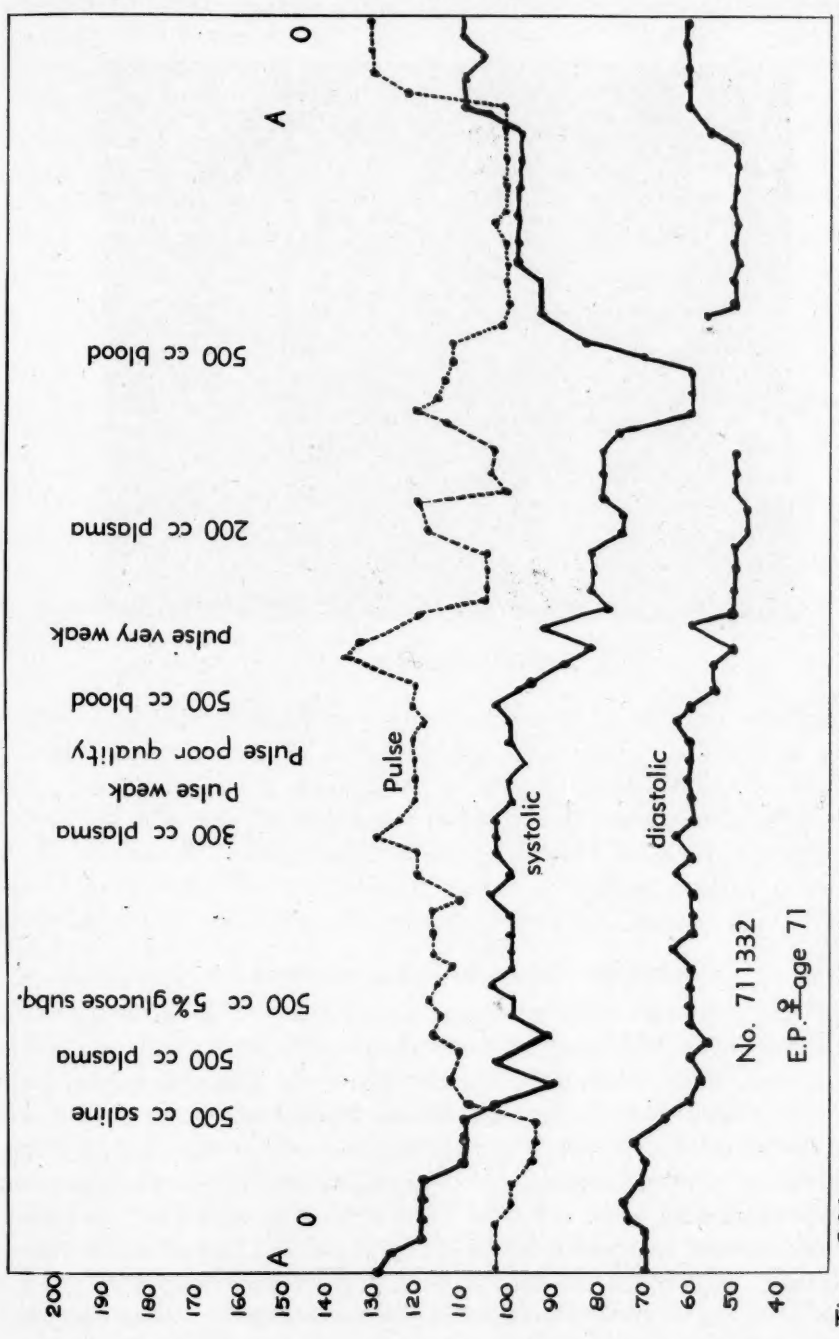

Time 3:00 15 30 45 4:00 15 30 45 5:00 15 30 45 6:00 15 30 45 7:00 15 30 45 8:00 15
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40
A O
500 cc saline
500 cc plasma
500 cc 5% glucose subq.
300 cc plasma
Pulse weak
Pulse poor quality
500 cc blood
Pulse very weak
200 cc plasma
500 cc blood
Pulse
systolic
diastolic
No. 711332
E.P. Page 71

Fig. 3.—Record of blood pressure, pulse, and intravenous fluids during anesthesia (Case 2).

during and after the operation. She died on the third postoperative day. The pathologic report was: (1) moderate amount of vacuolated liver cord cells characteristic of dissolved fat, congestion and atrophy of parenchyma also noted (some of these findings apparent in the photomicrograph, Fig. 4); (2) some congestion and patchy atelectasis of the lungs; (3) evidence of recent abdominal operation with gastric resection.

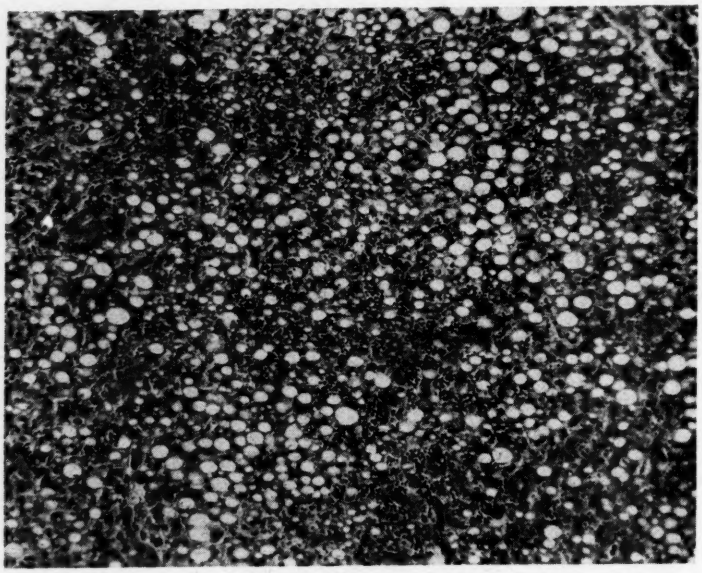


Fig. 4.—Photomicrograph of a section from the liver (Case 2).

Other case histories of this general type could be recorded, and their occurrence within a relatively brief interval served to focus attention upon the inadequacy of the dietary preoperative preparation in such instances. Since the development of a more formal dietary management and with the application of other methods of nutritional preparation outlined in the text of this essay, many patients with weight loss in excess of that reported in cases 1 and 2 have been successfully carried through correspondingly major operations.

MORE SPECIFIC STATEMENT OF THE PROBLEM

This study is essentially a clinical investigation. The selected critical control experiments, which can be undertaken by the investigator prosecuting his researches in the laboratory, are not, therefore, available in this study. Proof of the thesis that adequate nutritional preparation of the patient is an item of the greatest consequence must, therefore, rest on the accomplishment of what can be achieved through its employment, especially with reference to an earlier experience when surgeons were content to hydrate their patients adequately, restore electrolyte balance, and adjust the hemoglobin values by transfusions. In a sense, the results have been so gratifying that one may say with a feeling of confidence that, granted adequate nutritional preoperative preparation, in experienced and practiced hands very few patients will

have to be denied operation on the score that they are too poor risks for operation. In other words, the essence of this thesis is that a satisfactory nutritional preparation of the patient will extend the benefits of surgery to a group of patients who in the past frequently have been denied surgery, on the basis that they were too poor risks. Furthermore, extension may be made without pyramiding the risks very much beyond that accepted for the standard-risk patient for a similar procedure. When, during an ever-broadening experience and with an improved orientation in the problem, the benefits of preoperative dietary preparation for the poor-risk patients became so apparent, it seemed reasonable to apply similar methods in a variety of less serious conditions.

In this clinical study, the only criterion for the establishment of a satisfactory objective test of the extent and length of the necessary preoperative nutritional preparation has been the trial and error method. The percentile loss of body weight has served as a satisfactory base line from which to project the length and extent of the preoperative preparation. It is admitted that critical controlled experiments in animals, on this score, would probably be helpful to establish more precisely the length of the necessary period of preoperative preparation. At the same time, however, it must be conceded that results obtained from such a study would necessitate quantitative reconsiderations in the light of species differences and disparities in body size. Fowler and Barer[1] noted that among 105 donors an average interval of 49.6 days was required for the blood hemoglobin value to return to normal after a single donation averaging 550 c.c., and 25 per cent needed nine weeks. Provision for ample iron in the diet shortened this interval somewhat. Studies on dogs bled repeatedly furnish quite different rates.[2] They are capable of regeneration from a severely anemic to a normal status within two weeks after cessation of the hemorrhaging procedure. The hemoglobin rise in these dogs was 5 to 6 Gm. per cent in two weeks, while man needed nearly 50 days to correct a 2 to 3 Gm. per cent deficit.

The interest of the surgeon in the nutritional aspects of patient care relates primarily, therefore, to patients with conditions remediable by surgery who have lost considerable weight, occasioned by the ravages of the disease or who, for one reason or another, present a nutritional deficiency. It is proposed to indicate that it is hazardous to subject patients who have sustained large weight losses to formidable operative procedures after mere restoration of water and electrolyte equilibrium and concurrent adjustment of the hemoglobin to a satisfactory value. It is proposed further to indicate that such patients may be prepared satisfactorily for operation by a feeding of a high protein, high carbohydrate, low fat diet. It is proposed to indicate what the nature of the disability is that constitutes the operative hazard in these patients. Further, the character of satisfactory dietary preparation will be discussed including suggestions for diets which meet adequately the demands of the preoperative nutritional preparation of the patient who has sustained a large loss in body weight. It is proposed to indicate that following satisfac-

tory nutritional preoperative preparation, patients who ordinarily are regarded as poor operative risks may undergo formal operations of magnitude without running risks far out of line with those borne by the standard good-risk patient. In addition to presenting the nutritional problems of the patient who has sustained a large weight loss, it is proposed further to consider the special problems of nutritional preparation of surgical patients with high-grade obstruction at the gastroduodenal opening. The problem of meeting the caloric needs and of preparing nutritionally those patients unable to receive nourishment other than by the parenteral route is to be discussed. The problem presented by bleeding ulcers of stomach and duodenum, with and without obstruction, and in the younger and older age brackets, is to be dealt with in this presentation. Suggestions are to be offered for the nutritional management of patients with disease of the biliary system, especially cases with common duct stone or stricture, or carcinoma of the ampulla or head of the pancreas. The nutritional aspects of a variety of conditions including hyperthyroidism, burns, empyemas, osteomyelitis and other suppurative foci, esophageal lesions (carcinoma or diverticulum), and neoplasms of colon and rectum will be considered. Dietary preparation for surgery in the rarer conditions of gastrojejunocolic fistula, regional enteritis, and ulcerative colitis will be mentioned.

AN EXAMINATION OF CERTAIN ASPECTS OF RELATED LITERATURE

Prior to experiments by Bernard[3] in 1848 indicating that the liver could manufacture sugar when no sugar was present in the diet, it was the prevailing consensus bulwarked by the opinion of the famous contemporary chemist, Jean Baptiste Dumas, that man, unlike plants, had no ability to synthesize bodily fats, proteins, or sugar from those in the diet. Bernard and Barreswil[4] exhibited to the French Academy of Sciences alcohol obtained from sugar, of hepatic origin, by fermentation with yeast. The animal had been fed on meat exclusively and this example refuted, therefore, the hypothesis sponsored by Dumas. In subsequent experiments[5-10] it was shown that an "animal sugar-forming substance" (substance animale glycogène) was present in the liver and was converted to sugar on standing—a material that he later isolated in pure form and which is known today as glycogen. This was found to be identifiable in certain liver cells by virtue of a wine red color-staining reaction with iodine.* He also noted during experiments involving the livers of animals in various conditions of nutrition and health that this substance was present in lessened amounts in starvation states. Glycogen had been independently isolated one year prior to Bernard's classical experiments by Hensen.[12] Bernard's theory, in the main, is essentially accepted today by modern physiologists, namely, that carbohydrates incoming via portal blood are stored in the liver as glycogen, released to the blood as glucose, and are ultimately metabolized to carbon dioxide and water. During the ensuing two

*Bock and Hoffman[11] observed that liver glycogen was stainable with Lugol's solution for visualization under the microscope, and is more prominent about central liver cells and scant or absent about the periphery.

decades after the discovery of glycogen by Hensen and Bernard, the subject attracted the attention of many workers, both pathologists and physiologists, and there was general agreement that the state of nutrition was the chief factor determining its presence or absence. In prolonged starvation it would nearly or completely disappear from liver of rabbits, dogs, guinea pigs, hens, and other animals and fowl. Contrarily, an abundance was present when the animal's diet consisted of a plentiful supply of nitrogenous substances and/or carbohydrate. Wolffberg[13] pointed out the significant fact that when the amount of sugar in the diet remains the same, but increased quantities of dried and pulverized flesh (protein) are fed, the glycogen content of the liver is augmented. In addition, Wolffberg,[13] Naunyn,[14] and V. Mering[15] observed an accumulation of glycogen in the liver after an "albuminous" diet, one relatively free from carbohydrate. It was appreciated that the ability of the liver to produce glycogen was dependent on the integrity and the normalcy of the hepatic substance, and that, therefore, a smaller amount would be, and was, present in conditions interfering with the parenchyma, as occurs in fatty livers. This was most marked where the fat content had increased at the expense of the protein component. Saikowsky[16] was unable to find glycogen in livers with fatty degeneration developing after phosphorus or arsenic poisoning. This may have been related in part to the often poor nutrition of such animals. Manassein[17] found the hepatic glycogen content low in febrile states where catabolic processes are accelerated. The anorexia associated with such states customarily leads to a depressed, rather than elevated, caloric intake, so that one could conceive of this representing a form of relative starvation.

Cohnheim[18] noted extensive fatty changes in the chronic wasting diseases as carcinoma, intestinal tuberculosis, and dysenteries. Fatty livers were commented on in noting these changes even in people without fat depots in the panniculus adiposus, mesenteric and omental fat; all depots of fat had disappeared but the fatty liver was still present. He felt these were true "fatty atrophies," that is ". . . the albuminous contents of the affected elements are diminished and partly replaced by fat. . . ." "Fat can and will be produced at the expense of the albumin of the tissue elements—but this represents a proportionate loss of functioning substances." He also commented that this effect can be completely neutralized and effaced with restoration of tissue albumin content, the appropriate remedial measure, but where it is allowed to persist, it is the beginning of the cellular and functional end. Afanassiew[19] presented an excellent experimental study of the problem with many enlightening observations concerning the effects of alterations of the diet on the macro- and microscopic appearance of the liver in dogs. In starvation there was noted a decrease in cell and nuclear size, with the major component of this decrement taking place at the expense of the protein-staining material, and the minor portion accountable by disappearance of some glycogen. Specimens removed after this period of starvation possessed, therefore, an increase in the number of fat droplets within the parenchyma. If a normal animal were fed on sugar or potatoes, preponderantly a carbohydrate diet, the glycogen content

of the liver cells increased but the alteration in cell size was not pronounced. Sustentation with blood fibrin did lead to an actual increase in cell dimensions, but with little attendant glycogen deposition. Alimentation with a diet almost wholly meat produced the largest hepatic cells and they contained the most material taking the stain for proteins. The cellular size alteration with the quality of the food ingested (carbohydrate or protein) was reflected in the liver/body weight ratios. In states of starvation this fell to as low as 1:41, whereas, in animals nurtured on a meat diet it rose to 1:18. The values obtained on the carbohydrate and fibrin diets were intermediate. Atrophy and hypertrophy of hepatic substance in response to dietary influences are apparently here demonstrated for the first time; the significance of this rather neglected phenomenon can hardly be overemphasized.

In the midst of a long and classical paper on glycogen, Pflüger[20] stated that from his observations of the livers of animals maintained upon high protein diets, he was convinced that the liver is an organ for storage of both protein and glycogen. No experiments are cited, and the conclusion appears to arise from personal observtaions.

Seitz,[21] a student of Pflüger, did perform probably the first crucial experiments to test his theory and showed that in ducks and chickens maintained upon high protein diets there was real enlargement of the liver and increase in its nitrogen content. Tichmeneff[22] completed an even more convincing bit of work in experiments on mice where he found even an increase in protein content of hepatic substance as determined by an increase in the tannic acid precipitable fraction.

Luck[23] stated that each one of the four fractional protein components of liver increased with the alteration from a low protein to high protein diet. This increase was in the order of magnitude of from 50 to 60 per cent. He believed that this was explicable, on the basis of his experiments, as both a hypertrophy and a hyperplasia with an actual increase in protein content per unit weight of tissue. All the liver proteins appeared to participate freely in the storage function.

As suggested previously, hepatotoxins other than starvation are capable of effecting gross histologic and functional changes in this organ. The agent most extensively studied by investigators has been chloroform. This has probably been related to the gratifying reproducibility of the experimental conditions and results, the correlation between duration of anesthesia (or more quantitatively expressed as the amount of the drug ingested) and the pathologic findings under controlled conditions, and finally to the experimentally induced situations which mirror so closely the disastrous clinical counterpart met with occasionally in patients anesthetized with chloroform. Casper in 1850, soon after introduction of the drug as a general anesthetic, associated the possibility of death some time after its use, with a delayed action of chloroform. Nothnagel in 1866 related evidence to show that chloroform might produce fatty changes in the liver. Case reports then appeared in the literature

suggesting that this drug was responsible for death as a delayed manifestation of its toxicity, in distinction to its recognized capacity for producing cardiac arrest during the period of any administration. Rosenbaum,[24] while investigating a number of agents injurious to the liver, found a depletion of hepatic glycogen after chloroform anesthesia. Rosenfeld[25-28] demonstrated that animals fed on carbohydrate were, in the main, less susceptible to all those drugs producing fat accumulations in the liver. It was his contention that after such a poisoning (chloroform) the capacity of the liver for either protein or fat metabolism was more seriously impaired than for carbohydrates. The injured liver cells he felt could utilize carbohydrate, but with this constituent exhausted, the cells starved and exhibited obvious damage. The body in its futile attempt to use fat ultimately led to the local deposition, encountered under such circumstances, in the liver. Finally, he thought that the detoxifying capacity (entgiftenden fähigkeit) of the liver was positively correlated with its glycogen content. Beddard[29] grasped the significance of this biologic information and translated the suggestions into clinical therapy. At that time anesthetization with chloroform was in common use among English surgeons. He counseled before surgery, and especially where there was the possibility of hepatic glycogen depletion, as in the case of "rickety or ill-nourished children," that the diet include excess amounts of carbohydrates. It is difficult to understand how such an intelligent analysis of the similarity between animal experimentation and observations in man could have been so generally ignored by the healing profession. Wells[30] studied in detail the clinical findings, gross and microscopic anatomic changes, and chemical alterations in a fatal case of delayed chloroform poisoning. Among other considerations he emphasized the presence of an increased percentage of fat in the liver. It was his suggestion that as in the Meyer-Overton theory of anesthesia, the lipids of the liver take up the chloroform, which acting as a cell toxin interferes with normal functions. The amount of chloroform withdrawn from the blood, he hypothecated, would be proportional to the hepatic fat content, and therefore when increased amounts of fat were present the greater would be the cellular intoxication. Opie and Alford[31-33] resumed the attack on the problem from the nutritional sector. Employing white rats, poisoned with accurately measured amounts of chloroform, they studied the effects of qualitative alterations in the diet upon the mortality rate and found those animals fed a high carbohydrate mixture acquired a significant degree of protection. A meat diet was less effectual and where the diet was largely fat, all animals died under the conditions of the experiment. Any diet including fat in the caloric content immediately raised the mortality rate for that group. Whipple and Speed[34] found while studying the effect on liver function of therapeutic doses of a group of anesthetics and narcotics that all were capable of producing demonstrable evidence of impaired liver function as measured by a dye-clearance technique. Chloroform was noted to produce the most severely depressed function in the group where ether, alcohol, paraldehyde, chloral, and urethane were also studied. In an earlier investigation, Whipple[35] had been able to produce regularly, with chloroform anesthesia, a

necrosis of the central portion of each hepatic lobule in dogs, roughly proportional to quantity of the drug administered, as had other workers, but was surprised to note the frequent absence of such phenomena in the fetuses of pregnant dogs exposed to chloroform. This protection seemed to last about three weeks, and ably protected animals exposed to chloroform anesthesia at any time during this interval. A hyperglycemia with both ether and chloroform anesthesia was recorded, and this was associated with a reduction in hepatic glycogen. Graham[36, 37] sought the cause of this increased safety to chloroform anesthesia during the neonatal period and related it to the abnormally high glycogen content of the puppy liver compared to standard values for adult dogs, a value which spontaneously falls to a normal one in about three weeks after birth. He secured evidence favoring this concept, by producing a postchloroform hepatic necrosis resembling that of adult dogs among puppies who had had their glycogen stores depleted by starvation or phlorization. Under these circumstances the increased resistance to the drug was no longer present. Four papers by Davis and Whipple, and Davis, Hall, and Whipple[38-41] shifted the emphasis from the beneficial effects ascribed to an increased carbohydrate intake and an augmented hepatic glycogen content to the role of protein in protecting the liver exposed to chloroform. This originality of approach to the problem of hepatic damage, including methods, ideas, and food substances tested is clearly set forth in these papers by the Whipple group—papers that merit the distinction and respect due all classics, but much credit is similarly due Ravdin and his associates for initiating the clinical application of this fundamental knowledge. The experiments performed were numerous, the results and conclusions often unequivocal and self-interpreting. Only a few of the observations that seem most pertinent are to be cited:

1. Starvation materially increased the susceptibility of animals to chloroform. "A maximal injury is to be expected."

2. Sugar or richly carbohydrate diets, skimmed milk alone, commercial casein alone, or in combinations with a cracker meal, fed but a few preanesthetic days to the animals furnished maximal protection to the liver. An acid digest of casein administered a few minutes prior to the exposure to chloroform vapors appeared to offer some protection. Proteins from gelatin, heart, and skeletal muscle had only slight protective action.

3. They clearly stated, "The hypothesis that glycogen protects the liver cell against the injury of chloroform will not explain all the observed facts," and concluded that other factors must play a role.

4. The benefits from carbohydrate in the diet during the repair of hepatic injury due to chloroform accrue from the protein-sparing action of the carbohydrate, by virtue of "conservation of protein split products."

5. A diet of bread and skimmed milk evoked the optimum repair after a standard amount of chloroform injury. Other diets of cooked muscle or organs were less efficacious. Diets of fat, offered no assistance (more than was present during starvation) to liver regeneration.

Interesting speculations are initiated by a rather detailed perusal of the appended protocols and discussions. There was a tendency to flabby clot formation and even prolonged bleeding from biopsy sites. Doyon[42, 144] had noted earlier a similar phenomenon after chloroform anesthesia. Whipple and Hurwitz[43] demonstrated that there was an impairment or cessation of fibrinogen formation by the liver after injury with chloroform. Brinkhous and Warner[44] were to complete the explanation thirty years later in terms of hypoprothrombinemia ensuing after chloroform anesthesia, a hypoprothrombinemia which fails to respond to vitamin K until the hepatic parenchyma has recovered. In addition, it was noted by Davis and Whipple that after celiotomy for liver biopsy there was often an impaired wound healing associated with the experiments employing limited diets. This occurrence probably was related both to deficient plasma proteins and to inadequate vitamin C intakes. A more complete handling of this aspect of the nutritional problem will be considered later. If the calories and composition of the diets of Davis and Whipple had been calculated, then been made both ample and isocaloric, it would have quieted the valid objections certain to arise, for a part of the hepatic necrosis after chloroform anesthesia appeared in animals on diets obviously inadequate calorically, and which hence might be expected to suffer in this situation by virtue of the inadequate nutrition, a factor known to influence most unfavorably the hepatic tolerance for this drug.

Glycogen and protein appear, therefore, to potentiate natural hepatic resistance. The mechanisms responsible for this could be several:

1. Both substances are lipotropic, with glycogen less effective, and merely displacing fat already deposited. Protein actively removes fat from the liver parenchyma.[45-50]

2. Each might restore materials vital for cellular metabolism, as for example in the specific sense of a detoxifying substance or as an as yet unrecognized nonspecific material.[51] Xanthine, or its sodium salt, was found to influence favorably the prevention of acute or chronic hepatic changes after exposure to the toxin carbon tetrachloride. Ravdin, Vars, and Goldschmidt[52] employed sodium xanthine and obtained some protection for the liver after chloroform anesthesia. They felt it was related to the local tissue reaction induced by this substance. Hepatic glycogen has been suggested as the source of the detoxifying compound glycuronic acid.[53-55] Miller, Ross, and Whipple[56, 56a] described a distinctly enhanced protective action with methionine and cystine in dogs made hypoproteinemic, fed these amino acids, and then exposed to chloroform. It was their impression that this was a specific action related to the SH group, sulfydryl radical, present in, and essential for, certain hepatic detoxification processes which tend to spare other enzymes, normally present, associated with oxidation-reduction systems in the liver cells, as glutathione for example. Chloroform may be inactivated by these systems which during the process exhaust the quantity of interacting compounds, particularly if partial depletion has obtained previously because of a deficiency state. This permits competition between chloroform and normal respiratory mechanisms thereby interfering with the oxy-

genation necessary to prevent hepatic necrosis and autolysis, or at least permitting a functional depression with the accumulation of bodily substances customarily eliminated and detoxified by the liver. Contrarily, an excess of the sulfydryl groups, indispensable for the synthesis of the detoxifying product, can be brought about with the addition of methionine or cystine to the diet, or more deviously, by feeding casein which contains these amino acids. With such a theoretical excess present the chloroform hazard actually, in experiments designed to test this concept, appeared nearly nullified. Beattie and Marshall and associates[220-222] have sought to evaluate clinically methionine as a therapeutic aid in patients with liver damage from infective hepatitis and one instance of carbon tetrachloride poisoning. The material was supplied to their patient orally and intravenously. Even admitting the limitations imposed by the meager quantity of data available, since the results achieved were so favorable in the patients appropriately selected for such therapy, the perhaps premature surmise is hazarded that in the near future this amino acid is destined to assume a truly vital role in the restoration of function to livers damaged, through fatty metamorphosis or other hepatotoxins, but not destroyed as in advanced cirrhosis and severe acute atrophy.

3. Glycogen by conversion to glucose could exert its well-known protein "sparing" action either at the source[32, 40, 57] and thus reduce the amount of protein autolyzed or in a more peripheral fashion and "spare" the conversion of amino acids to energy units, permitting a more liberal utilization in the normal anabolism. More words than wisdom have been written in frequent and occasionally bitter polemics which have attempted to resolve, either on paper or in the laboratory, these issues cited, into primary effects and contributing action.

Moise and Smith[58, 59] found protein more effective than carbohydrate as a substance for inducing hepatic protection after exposure to chloroform. Goldschmidt, Vars, and Ravdin[60] then explored this possibility, namely, that the protein component of the diet is of more fundamental importance than the carbohydrate fraction in the development of hepatic protection against chloroform anesthesia. They studied the effects of this drug on white rats, "because of the ease of attainment of adequate maintenance and growth on diets predominating in one or another of the foodstuffs," and then fed several variations of these diets to the animals, including those with very high carbohydrate, mixed carbohydrate, protein and fat content, high protein low fat or high fat, and high fat without protein. After a prolonged subsistence on the selected regimen the animals were exposed to chloroform vapors in a standard fashion and then sacrificed at the end of twenty-four hours. The livers were studied chemically for glycogen and fat, and microscopically for both these as well as the cytologic reactions of degeneration and necrosis. The authors wisely refrain from sweeping generalizations about these experiments but do propose the following interpretations of the supplied data:

1. Within a constant range of hepatic lipid content, in animals on similar protein intakes, a high hepatic glycogen content per se fails to provide protection.

2. Under their experimental conditions, a direct linear relationship exists between hepatic lipid content and the incidence and severity of the damage to the liver following chloroform anesthesia.

3. This effect is independent of the glycogen content but can be attenuated by a previous feeding of a high protein diet, and obtains in instances of high hepatic lipid content. Conversely, starvation aggravates the damage normally accomplished by a chloroform anesthesia, an effect additionally potentiated by a high lipid content in the liver of the starved animal. Casein, as in the experiments of Davis, Hall, and Whipple,[41] was the protein selected to fortify these diets. Messinger and Hawkins[61] confirmed the work of Schifrin,[62] who noted a minimizing of the arsphenamine injury to the liver in animals fed a protein as compared to a fat diet. Histologically, regeneration was more rapid and complete with the former. In addition, dogs on the high fat diet exhibiting manifest liver injury (elevated icterus index) and a reluctance to eat promptly displayed an improvement and regression of the hepatic dysfunction when changed to a high protein or carbohydrate diet. Miller and Whipple[63] studied the effect of chloroform on animals made hypoproteinemic by plasmapheresis or diet and came to the conclusion that the severity of the injury to the liver in these dogs after such anesthesia paralleled the depletion of liver and body protein. Quite minimal insults from light chloroform anesthetization for short periods of time (fifteen to twenty minutes) were fatal to the majority of such canines, while control animals tolerated ninety minutes of such exposure with but little liver injury. This enhanced susceptibility in the depleted dogs could be corrected, it appeared, at least in part, and at times completely, by a single large feeding of protein (meat) thirty-six hours prior to the anesthesia. Dogs depleted of proteins by plasmapheresis uniformly gained some protection against liver damage when nourished with a richly protein diet. They could not tolerate the same amount of chloroform as normals but convalesced significantly superior to those depleted animals not so selectively alimented.

There may be no satisfactory single explanation available, on the basis of our admittedly limited present knowledge, and assuredly it is difficult to arrive at the common denominator for the effects produced by chloroform anesthesia in a liver with a high lipid concentration—actions which are potentiated by starvation or hypoproteinemia, and inhibited either by a high hepatic protein content or feeding before the exposure of a full protein dietary supplement. However, at the risk of indulging in oversimplification, the impression exists that this phenomenon so intimately related to cellular metabolism may be but a manifestation of anoxia. In partial support of this thesis is the recognition and general acceptance that chloroform interferes with oxidation—reduction potentials (vide supra). Additionally, Goldschmidt, Ravdin, and Lucke[64] found that vaporizing chloroform with oxygen rather than air decreased the damage produced by this drug on the liver, and that this deleterious action could be inhibited (by breathing high concentrations of oxygen) even where livers had a high lipid content. Schneedorf and Orr[65] found a depression of the liver function, bile formation, with anoxia and a prompt

return at an increased rate after the administration of 100 per cent oxygen. It might be predicted that since most of the blood coming to the liver has passed through a set of capillaries and is already venous, that as it traverses the second set, the oxygenation, being additionally reduced, is at a critical level and only a meager oxygen reserve remains available. Warren and Brannon[66] obtained blood directly from the hepatic veins in man and after measuring the oxygen content found it was lower there than in samples obtained from the auricle. In addition, the situation is made even more critical, and the tolerances further reduced, because in this tissue with an, at best, low tension of the oxygen essential for anabolism, there exists according to Bradley[67] the highest rate of intracellular proteolysis (catabolism). This contention is clearly substantiated by the experiments of Addis, Poo, and Lew,[68] who noted that of all the body proteins, liver had the largest percentage loss during a brief fast. Here, with protein absent from the daily intake, the counterbalancing of autolysis by synthesis is at a serious disadvantage.

This summary of a proposed theory relating ultimately the ill effects of chloroform to local anoxic states is, therefore, offered.

1. Fat contributes to the anoxia by two mechanisms:
   (a) It attracts and holds an abnormal amount of chloroform compared to the other tissues with lower fat solubility coefficients, and hence a greater quantity of this drug is available to depress the respiratory enzyme system, more completely, and for a longer interval of time.
   (b) It acts as a diluent of other constituents and thereby increases the diffusion distances for entering oxygen and outgoing, frequently toxic, products of metabolism.
2. Glycogen favors adequate oxygenation through its mildly lipotropic action and by increasing with its protein-sparing power the quantity of protein available for cellular metabolism.
3. Protein prevents anoxia because of its strongly lipotropic capacity and because the natural respiration of a normal cell depends primarily upon an adequate available complement of protein.

The conclusion is also reached that these apparently pathologic states are likewise reversible, under appropriate conditions, and are interpretable, therefore, as exaggerated expressions of a labile and dynamic equilibrium. The effects of high or low fat, carbohydrate, or protein diets find representation in functional and, frequently, microscopically visible states, often reversible, and whereas the intake of a high protein-carbohydrate diet has the capacity to shift this reaction in the direction of intracellular synthesis and a normally functioning, nonpathologically involved mechanism, unfortunately quite the opposite obtains when the liver is injured by semi- or starvation states and other more powerful chemical hepatotoxins.

LITERATURE CORRELATING NUTRITIONAL CARE WITH CLINICAL MATERIAL

An appreciation of the importance of nutrition in clinical cases which resemble the experimental conditions just described has not been totally lack-

ing but does seem, compared to the possible significance, to have been disproportionately meager. Often the emphasis has been preponderantly on the dysfunction from an hepatitis associated with biliary tract disease.[69-76] Graham[69] re-emphasized under such circumstances the significance of faulty dye clearance by the liver, at the time of cholecystography. When seriously impaired function was demonstrated, in this fashion, the patient was prepared for several days with additional amounts of glucose intravenously. With such therapy he was able to curtail the mortality of cholecystectomies at his clinic by 90 per cent.

It does not seem pertinent to discuss at length the several papers which tend to obfuscate issues at best already somewhat less than clear. For instance, Soskin and Hyman[77] in an article abstracting a number of papers by Soskin on this problem, without an inferred or direct reference to the total caloric intake, stated that intravenously administered glucose is superior to oral carbohydrate, "to protect a damaged liver by means of deposition of glycogen therein." Sears and Banks[78] expressed a similar conviction in the matter of intravenous versus oral feeding of sugar, and both groups are categorically certain of the prime, almost exclusive, importance of carbohydrate. . . . "Acute and chronic destructive and degenerative processes of the hepatic parenchyma are best treated with large amounts of carbohydrate," to quote the former group, and "cellular repair of the liver is best facilitated by a carbohydrate diet," affirmed Sears and Banks. These two statements ignore the most basic fundamentals of tissue healing, and the local necessity for protein, for under such circumstances as those outlined, the sole source of nitrogenous material for regeneration would be from endogenous metabolism. This admittedly contributes a component to the anabolism, as indicated by Davis, Hall and Whipple,[41] but the addition of protein to the dietary intake ordinarily supplies the preponderant fraction of the quantity required. Also, the unqualified statements of these groups relative to the superiority of intravenously injected glucose over that provided through the oral route overlook the stringent caloric limitations imposed when venoclysis is the sole avenue for nutrients to enter. It is barely possible to provide the minimum caloric needs for basal conditions in adults by this method, and to conceive of effecting any appreciable storage is not heeding reality. Until the work of Goldschmidt, Vars, and Ravdin,[60] this general plan represented approximately the maximum nutritional preparation of surgical patients with biliary tract disease. In 1939 this group called attention to the necessity of providing extra protein in a diet to be fed preoperatively. The diet recommended contained 74 per cent carbohydrate, 20 per cent protein, and 6 per cent fat in sufficient quantity to yield 3,000 calories daily in three meals and three interval feedings. The high carbohydrate content was found to be well tolerated by patients. The protein in large measure consisted of casein in the form of cottage cheese, skimmed milk, and Casec.* Biopsy specimens, obtained from patients given this diet five or more days preoperatively, contained uniformly less hepatic fat than material

*A proprietary preparation of Mead Johnson and Company, Evansville, Ind.

from a comparable group of patients not given this diet. An inverse relationship between glycogen content and liver fat was not encountered, that is, several instances of a heavy degree of fatty infiltration were associated with the highest hepatic glycogen concentrations.

Many investigators and clinicians interested in the problems of hyperthyroidism have related the thyroid storms and deaths postoperatively to hepatic damage or correlated hyperthyroidism with hepatic failure.[79-88] Shaffer[89] in the autopsying of patients with hyperthyroidism found convincing evidence of histologic changes, especially loss of liver substances and fatty infiltration. The hippuric acid liver function test has been employed in the detection of hepatic dysfunction developing in this condition.[80, 88] Preoperative clinical improvement in the patients was paralleled by a return of the conjugation values toward normalcy and postoperatively pathologic levels were common. It has been appreciated for many years that the administration of thyroid hormone to animals resulted in a low level of hepatic glycogen,[90] that an elevation of the level was difficult to obtain,[91] and that such animals had an increased susceptibility to hepatotoxins.[92] The customary method of feeding hyperthyroid patients was presumably influenced unfortunately by this, therefore preparation emphasized only carbohydrates in the preoperative nutrition. Attention might profitably have been focused also on the tremendous protein needs developing under such circumstances.

Coleman,[94] and Boyce and McFetridge[95] at about the same time found that patients with apparently normal hepatic function sustained a drop in function, occasionally to a marked degree, regardless of the variety of anesthesia, after the relatively simple operations like elective hernioplasties or appendectomies. In some instances wherein hepatic damage was noted preoperatively, a dangerous impairment of liver function was exhibited after anesthesia and surgery. Ravdin[96] stated, "When the concentration of liver fat increases about the normal, and the reserve stores of protein are seriously reduced, liver necrosis is apt to occur when the patient is subjected to a variety of anesthetic agents, regardless of the hepatic glycogen level." Abels, Rekers, Binkley, Pack, and Rhoads[97] studied fifty proved cases of carcinoma in the gastrointestinal tract. Each patient was examined for evidence of hepatic dysfunction by means of eight tests. Ninety-eight per cent displayed an abnormality in two or more tests, 86 per cent had three or more tests in the pathologic range. Among twenty-five normal adults investigated by the same tests for hepatic function, two individuals had a maximum of two tests recording abnormal values. The tests employed were determinations of the plasma prothrombin, serum bilirubin, serum proteins (total and fractionation into albumin and globulin), plasma vitamin A level, urinary excretion of glycuronates, mean corpuscular volume of erythrocytes, urinary and fecal excretion of urobilinogen, serum cholesterol, and cholesterol esters. The advantage of selecting multiple tests is apparent. Any one alone provides but a crude index of the functional state of the liver, whereas, with a number of tests one can secure information on the numerous independent physiologic functions of this organ, and thus values can be secured which more closely approximate the actual hepatic capacity.

This demonstration of a depression of two or more indices of hepatic function, in so large a percentage of the total number of patients with gastrointestinal disease, seems particularly significant. Frequently it is precisely this individual, with such a case history, laboratory findings, and diagnosis of a gastrointestinal cancer, who requires a very major type of surgery. The failure to recognize, treat, and correct such hepatic derangements is certain to pyramid the risks of anesthesia and of the operative manipulations, to hamper of wound healing, and thus ultimately to increase the mortality rate of this group.

DISCUSSION OF MECHANISMS OF HYPOPROTEINEMIA

Hepatic dysfunction and the fatty liver developing in surgical patients are problems unquestionably of great prognostic significance; their remedy is of paramount therapeutic consequence. At times, the many perplexities connected with an analysis of the mechanisms producing hypoproteinemia appear to be closely woven into these same considerations; in other instances hypoproteinemia develops from diverse causes. On all occasions it arouses an equivalent interest and is as important to the whole dietary problem as hepatic dysfunction and the fatty liver. The following is proposed to furnish some orientation into the mechanisms concerned with the development of hypoproteinemia:

Increased Rate of Catabolism.—Hypoproteinemia may result from an increased rate of catabolism, that is, the combustion of body protein takes place more rapidly than normal and, unless compensated by augmented intake, at the expense of protein stores. The increased excretion of urinary nitrogen, noted during febrile states, is the best example. Here the wasting process is rapid and promptly leads to a negative nitrogen balance, unless treated. It is rather unorthodox to consider hyperthyroidism in a discussion on hypoproteinemia, yet here too the protein needs are sharply increased. More fortunately than in the hyperthermias, where anorexia is the rule and secondarily reduces the protein intake, here the appetite is customarily enhanced and some compensation of intake, therefore, takes place. The adjustment is frequently inadequate, however, because the tempo of metabolism under the driving influence of thyroxin is so rapid that destruction of the individual's own tissues takes place. The percentage of total body weight lost recently is of the gravest significance in the preoperative evaluation. Therefore, the diet of the thyrotoxic patient should provide increased amounts of all basic elements with the emphasis on the protein and carbohydrate components. The metabolic problem in hyperthyroidism is complicated further by the depression of hepatic function and an increased sensitivity to hepatotoxins (vide supra). This is, therefore, another reason to include in the diet ample supplies of proteins with a high biologic value that body repair and regeneration be effected with the greatest expediency.

Increased Rate of Loss.—Hypoproteinemia may result from an augmented rate of protein loss. For example, early from a burned area copious quantities of protein are lost in the fluid weeping from the myriads of injury capillary walls no longer impervious to protein seepage. Large amounts also are

sequestrated into the tissues locally, yet probably most of these eventually accumulate back in the circulating blood via the lymphatics. Temporarily, however, their absence does contribute to the acute hypoproteinemia of burns. Later, in the history of a burn, protein is lost both by the exudation of plasma from extensive, granulating unepithelialized burned areas and through the richly protein cellular discharge of leucocytic elements from this site. And the stores are depleted still more by the increased requirements relative to healing and repairing the cutaneous defects produced by the burn.* Other frequent surgical problems with abnormal protein loss are: following hemorrhage, during peritonitis, in small bowel intestinal obstruction (particularly the strangulating varieties), and in chronic ulcerative lesions of the large and small bowel. Less obvious examples are found in the protein character of exudates from abscesses and empyemas. The purulent discharge from a spacious suppurative pleuritic cavity may amount to several hundred cubic centimeters daily of fluid with a protein concentration of 8.1 to 21 Gm. per cent and may contain 4.6 to 11.5 Gm. per cent of albumin.[98, 99] Thus, much protein is commandeered from the circulating stores and depots, which a febrile and anorexic patient can ill afford, either in terms of his reduced dietary intake or by virtue of the depressed hepatic function associated with such infectious states. The loss may be largely renal, as in nephritis, nephrosis, or amyloid disease. A single large or multiple smaller decubitus ulcers are capable of easily producing a serious unfavorable nitrogen imbalance. The tremendous amount lost by repeated paracentesis for ascites simulates closely the experimental plasmapheresis technique. Quite as easily it is capable of inducing severe hypoproteinemic states. In constrictive pericarditis with ascites treated by repeated aspirations the hypoproteinemia has been wrongly stated to be of hepatic origin. The protein content of such fluid is customarily small (1 to 2 per cent) but because of the several liters removed at each sitting, the total protein loss is large, especially since it is predominantly albumin. Therefore, actually, the liver may be producing the colloid protein at better than a normal pace.

Decreased Protein Intake.—Hypoproteinemia may result from a nutritional deficiency. That is, it may develop through poor selection, unavailability (war edema), a frank reluctance or disinclination to partake of food, or some defect in absorption as characterizes conditions like sprue, pellagra and occasionally pernicious anemia, the nonspecific diarrheas of infancy or bacterial ones of adulthood, and gastrocolic and high intestinal fistulas.

Reduced Capacity of Fabrication.—Hypoproteinemia may result from a reduced capacity or actual failure of protein fabrication by the liver. Acute, subacute atrophy, biliary (Hanot's), and portal (Laennec's) cirrhosis are the outstanding examples of this mechanism. Actually, the protein synthesis is probably depressed to varying degrees by all agents inducing a hepatitis, that is, sulfonamides, arsenicals, anesthetics, shock, bacteremia, virusemia, septicemia.

It is admitted that this outline which has been proposed for the several fashions by which hypoproteinemia may develop possesses inadequacies. For

*An additional expression of the thermal injury could be an actual hampering of conversion, by the body, of amino acids to fabricated proteins, as proposed in the post-traumatic theory of abnormal nitrogen loss.

instance, the reader may well recollect mechanisms producing hypoproteinemia which have not been included. Also, at times, certain conditions may seem to have been arbitrarily placed under one heading rather than another. In addition, and this is to be emphasized, one or more causes for depletion may coexist and simultaneously effect unfavorably the plasma proteins. That is, low values ascribable to an inadequate caloric intake will be secondarily reduced through the agency of ulceration, hemorrhage, and sepsis, and tertiarily depressed by a concomitant reduction of hepatic function. Even with these imperfections inherent in this outline, it is felt that by so cataloguing the broad range of events contributing to the development of hypoproteinemia, its genesis will attain a clearer appreciation.

DISCUSSION OF THE EFFECTS OF HYPOPROTEINEMIA

Many ills and complications of postoperative convalescence are said to stem from hypoproteinemic states. The following are the more clearly chargeable to such a reduction in plasma protein. There may be impaired wound healing or even disruption. Delayed intestinal motility, even intestinal obstruction, and anastomotic stomal difficulties have been noted. Edema formation can supervene, and related to this are quite likely some of the postoperative bronchopneumonias. A decreased resistance to infections with a reduction in antibody formation has been described. Probably also a decreased tolerance to shock-producing circumstances exists. Certain chronic anemias appear related to an inadequate protein intake. Other miscellaneous conditions have been ascribed to this condition. Clark, after studying the effects of diets on wound healing, inferred from feeding a high protein diet to dogs that this abolished the quiescent or lag phase in their wound healing. Harvey and Howes rather felt that the inception of the healing process did not occur any sooner on a high protein diet, containing 80 per cent casein by weight, but believed the velocity of fibroblastic growth was more rapid and that maximum healing was reached sooner under these conditions. The work of Clark,[100] and of Harvey and Howes,[101] is, therefore, a somewhat practical application of the fundamental researches of Osborne and Mendel[102] and of Rose.[103, 104] These workers clearly indicated the utter essentiality of certain amino acids for normal growth processes. Arey,[105] reviewing the problem of wound healing, concluded that many of the most important factors associated with repair were more or less directly related to or dependent upon a diet high in protein. Thompson, Ravdin, Rhoads, and Frank[106, 107] confirmed the finding of earlier workers of delayed fibroblastic proliferation in hypoproteinemic dogs, but were able to prevent this reparative delay by elevating the colloid osmotic pressure, after the incision was made, employing lyophilized plasma. Clinically there is recorded an increased incidence of wound disruptions in hypoproteinemic individuals. Rhoads, Fliegelman, and Panzer[108] related the mechanism of delayed wound healing in hypoproteinemic animals directly to the reduced colloid osmotic pressure. This, they believed, was the most satisfactory explanation for normal fibroplasia in dogs, made hypoproteinemic (by plasmapheresis or other methods), in whom the total colloid osmotic pressure was raised to

approximately normal values by the intravenous injection of the metabolically inert material, acacia. Sokolov[109] and, somewhat later, Lanman and Ingalls[110] indicated the importance of adequate amounts of vitamin C for normal wound healing. They felt this consideration was an important biologic factor in normal regeneration. Taffel and Harvey[111] confirmed these findings. Hartzell, Winfield, and Irvin[112] were inclined to credit hypoproteinemia with at least as an important a role in the reunion of operative sites. While appreciating the value of vitamin C in repair, they pointed out in their cases that in each instance of disruption, hypoproteinemia was associated. A rather interesting possible causal relationship between vitamin C deficiency and protein genesis was hinted at in two papers by Levine, Marples, and Gordon.[113, 114] An inability to metabolize the amino acids tyrosine and phenylalanine, which developed spontaneously in an infant, was corrected, they noted, by the use of ascorbic acid. In summary, it seems reasonable to opine that with either a plasma protein lack or cevitamic acid deficiency, wound healing is retarded; with both reduced, the felony is compounded.

Jones and Eaton[115] were among the first to relate malfunctioning gastroenterostomy stomas to postoperative nutritional edema. They appreciated that the latter was related to the malnutrition, starvation, hemorrhage, and purulent discharges which were not uncommonly the lot of surgical patients. Unfortunately, the incomplete, and hence with respect to tissue repair well-nigh valueless, protein, gelatin, was selected for fortifying the proposed corrective diets. Mecray, Barden, and Ravdin[116] noted a profoundly delayed emptying time occurring in intact stomachs or the residual pouch after resection. They suggested this was caused by hypoproteinemia. It was felt that the "vicious circle" effect (Barden Ravdin, and Frazier[117]) after gastroenterostomy could be relieved in certain instances by transfusions. Davis and Getzoff[118] found instances, simulating adynamic ileus they believed to be caused by hypoproteinemia, which were corrected by transfusions.

Starling[119] was the first to hypothesize a fluid circuit between the blood stream and the extravascular spaces in which the distribution of liquid was regulated largely by a finely adjusted balance between hydrostatic pressures and the colloid osmotic forces. The range of normal values of the plasma proteins producing this force, according to Furey,[120] is:

	AVERAGE	RANGE
Total proteins	7.36	6.2 to 8.1
Albumin	4.92	4.1 to 5.8
Globulin	2.40	1.7 to 3.5

Per gram, the albumin fraction contributes 5.5 mm. of mercury and the globulin fraction 1.4 mm. of mercury osmotic pressure, under normal states of hydration.[121, 122] However, when the plasma proteins are reduced in concentration, as in hypoproteinemia, each gram has less osmotic force, and as might be anticipated when there is increased protein concentration, as in dehydration, each gram exerts more force than it does at normal concentrations.[123-125] A total osmotic force of circa 17 mm.[126] of mercury is necessary to prevent

edema formation with normal hydration. Bruckman and Peters[127] noted edema when albumin concentration fell below 3 Gm. per cent, with adequate hydration. Moore and Van Slyke[128] stated the critical concentration of total proteins, below which edema is likely to develop, is 5.5 ± 0.2 Gm. per cent and for albumin 2.5 ± 0.2 Gm. per cent. Weech and Ling[129] and Lepore[130] found it difficult to produce edema in dogs or human beings with very low plasma protein levels, where a severe sodium ion restriction was effected. Others[131-133] have verified this conclusion, and we have repeatedly confirmed and made use of this fact to prevent or abolish edema formation in hypoproteinemic individuals, where it is difficult or impossible temporarily to restore the plasma proteins because of other considerations. One can hardly sanction the administration of sodium chloride in such liberal quantities as has been advocated, and as may prove necessary, to maintain the plasma chloride level at or above 560 mg. per cent, in the group of patients with low cardiac reserve and/or with uncorrected hypoproteinemia. In our experience this has proved more hazardous than the deliberate development, judiciously tended, of a mild state of dehydration and dechlorination. Usually this can be easily effected by a reduction in the daily supplement of dietary or parenteral sodium chloride. To be sure, since sodium is really the malefactor similar restrictions must be imposed on the use of sodium as the bicarbonate for an antacid or in conjunction with sulfonamide therapy. In the majority of instances with such limitations of chloride and fluid a satisfactory balance is readily struck and future adjustments are made on the basis of the patient's day-to-day weight, plasma chloride level, presence or absence of edema, and related complications. Clinically, such short periods of mild dehydration and dechlorination, carefully supervised, appear to evoke no serious secondary manifestations, while visibly correcting an edematous state and holding it in abeyance until the danger no longer exists of postoperative complications such as impaired wound healing, bronchopneumonia, intestinal stasis, etc.

Scrutiny of the protocols and data of Davis and Whipple[38-41] and Mecray, Barden and Ravdin[116] shows recorded a high frequency of distemper in animals made hypoproteinemic. Whipple stated, "Plasma depleted dogs are even more susceptible to infections (than anemic ones) and many of the dogs used in the earlier experiments died of abscesses, septicemia, endocarditis, and related conditions." The antibody production necessary for opposing infectious processes requires protein in the form of globulin, and is, therefore, influenced by the depreciation occurring in this fraction during many hypoproteinemic states. Such a curtailment would be reflected in a diminished capacity to resist nocent bacterial invasion. The experimental evidence favoring this viewpoint has been discussed by Cannon and associates.[134, 134a] His conclusions afford at least a partial confirmation to the theory since rabbits, after a plasmapheresis depletion of their protein stores, exhibit a definitely decreased capacity to produce antibodies. Also, several other types of small animal experiments designed to test this thesis have yielded confirmatory data.

Other miscellaneous pathologic conditions have been directly or inferentially related to hypoproteinemic states. Hahn and Whipple[135] found that ani-

mals maintained anemic by bleedings produced more hemoglobin when diets contained ample amounts of protein than when they contained low amounts, despite an adequate iron complement in both experiments. Orten and Smith[136] and Orten and Orten[137, 138] found that a mild chronic anemia developed in rats fed a low protein diet, and controls with sufficient protein in the diet had normal blood findings. When the protein content was maintained reduced, but the total number of calories raised, the chronic anemia persisted; increasing the protein content (lactalbumin) with caloric values lowered promptly restored the blood picture to normal. Iron additions to the diet were without effect. Bethell,[139] observing anemias occurring in normal pregnancies, was inclined to believe they were related to an inadequate amount of dietary protein, and noted favorable responses when this component was increased. Studies[74] in progress now at the University of Minnesota Hospitals, upon the obstetrical and gynecological services, rather confirm this impression.

Chang[140] measured the blood volume in patients with low plasma protein values and an associated nutritional deficiency and found these volumes reduced. This has been corroborated in a limited study of our material. This finding has been amply confirmed in experimental animals by Holman, Mahoney, and Whipple,[141] and Elman and Davey.[142] Such a contraction of the total quantity of circulating blood would be likely to exaggerate any shock-producing mechanisms attendant with surgical procedures. De Navasquez[143] described hepatic changes with fatty metamorphosis and brown atrophy of the heart in a case of nutritional edema with hypoproteinemia; Davis and Getzoff[118] consistently demonstrated with the hippuric acid tests, decreased liver function in hypoproteinemic patients.

Less tangible but nonetheless impressive is the characteristic improvement in the patient's general appearance and reaction, amounting almost to a mild euphoria, shortly after conversion from a negative to a positive nitrogen balance. Patients who have been a long time autocannibalistic become indifferent to their needs and surroundings and ultimately incapable even of the efforts required for existence. Others[201] have noted a similar improvement in depleted patients after increasing the nitrogen intake.

In recapitulation, therefore, it can be stated that the causes of hypoproteinemia are legion; the effects of hypoproteinemia are already multiple with many as yet probably unidentified or/but vaguely appreciated. The complexity is heightened, too, by the rather likely consideration that hypoproteinemia arising from one cause may add to its own evil and perpetuation through remote influences, that is, a depression of fabrication in the hepatic substance and anorexia after a local loss from an extensive burn. However, with this knowledge, albeit limited at our disposal, it is now possible to undertake a more rational and less empirical therapy for these major problems of the fatty liver, hepatic dysfunction, and hypoproteinemia.

Starting with the transient supply of proteins with which we are born, and ever thereafter, our bodies require external sources of plant or animal protein for survival. These we eat, digest, absorb, and utilize for energy or refabrication into a specific species protein. Visible dissolution of the ingested

protein begins in the stomach, but under the influence of powerful proteolytic intestinal enzymes this nutrient is fractured eventually into short peptides and amino acids. These, more commonly as the latter than the former, are absorbed into the portal circulation and there serve to provide energy, or to synthesize the bodily proteins of plasma and tissue. All the albumin, fibrinogen, prothrombin, and much of the globulin are formed in the liver from these absorbed products of digested protein. Some globulin is apparently manufactured by the reticulo-endothelial system outside the hepatic substance. Another fraction of the circulating amino acids or more complex aggregates is employed to construct hormones, other protein-containing secretions, and the cellular blood elements. Those amino acids not required intact for these functions are deaminized chiefly by the liver, with the NH_2 group developing into ammonia which then combines with CO_2 to form urea. The fatty acid residue, when oxidized, then supplies energy directly or if the amino acid precursor was glycine, alanine, arginine, aspartic, serine, cystine, glutamic, hydroxyglutamic, or proline, glucose may be formed and burned or stored as glycogen. The work of discovering which of the twenty odd amino acids were indispensable occupied many of the leading biochemists for years. As a result of the work of all the investigators, Rose[103, 145] was able to present a classification dividing the group into the two categories, essential and nonessential, for growth and maintenance. This work, done in rats, strictly speaking is therefore known to hold only for them, but the best information available now suggests that much the same partitioning is valid for man.

ESSENTIAL	NONESSENTIAL
Arginine	Glycine
Methionine*	Alanine
Isoleucine*	Serine
Leucine	Aspartic
Lysine	Glutamic
Valine*	Proline
Phenylalanine*	Hydroxyproline
Tryptophan*	Tyrosine
Threonine*	Cystine
Histidine†	Hydroxylysine
	Norleucine‡

Since these ten amino acids are essential for normal cellular growth, the quantity in which they are present is probably a limiting factor in plasma protein regeneration. Certain experiments of Madden and Whipple,[146] in which basal diets were augmented with various combinations of essential amino acids, are strongly suggestive.

By means of the process of transamination, that is, the conversion of keto acids R-CO-COOH to amino acids R-CH(NH_2)-COOH, within the cell substance, certain amino acids are synthesized in the body, thus providing a partial independence in protein fabrication. Unfortunately, all amino acids cannot be

*The quantities of these amino acids required for promoting growth are greater than for the unstarred group. Absence or severe limitation in amount of any one of these starred acids seriously limits growth.

†This amino acid may not be essential in man.

‡This is included in some lists as essential for growth and maintenance.

thus developed by the body. Therefore, we may define an essential or indispensable amino acid as one that the body is incapable of synthesizing in quantities ample enough to insure maintenance and normal growth. It is self-evident, therefore, that any contemplated diet conceived as the method of correcting a negative nitrogen balance must possess all the essential amino acids and in particular abundance those necessary for growth. Regardless of the total quantity of protein provided and eaten, protein deposition cannot be successfully effected with a single essential amino acid absent. With an essential amino acid lacking, the majority of the absorbed nitrogen is excreted in the urine. This transpires despite almost any degree of need for nitrogen retention, to form protein, that may exist in the animal at the time. In the final product of protein synthesis, the content of the several amino acids varies, but the eventual assembly into a functioning entity occurs only minimally, or not at all, unless every component part, in the required amount, is available. Those foods, therefore, which contain all these amino acids in concentrations more closely approximating that in tissue protein are more likely to be effective in protein regeneration. While no sweeping conclusions are permissible regarding the superiority of animal over plant proteins, since the composition of the former tends, in general, to mimic that of the new protein more closely than the latter, better results can be anticipated with such a feeding. Kerr, Hurwitz, and Whipple[147] in 1918 were the first to present evidence that diet is a potent factor in the regeneration of plasma proteins. In the years since, many investigators[148-156] from Whipple's laboratory have analyzed a variety of foodstuffs regarding their capacity to promote protein formation in dogs with a controlled hypoproteinemia. The animals were maintained in this state for as long as a year by repeated plasmaphereses, so graduated as to insure a close approximation of plasma protein content to 4 Gm. per cent. Since such animals produce a relatively constant minimal amount of plasma protein when on a fixed, standard, limited protein diet, any increase in plasma protein with the addition of other kinds of proteins or combinations of pure amino acids permits a calculation of the effectiveness of each test substance. Actual values can then be obtained by noting the actual number of grams of plasma protein obtained from feeding 100 Gm. of the test protein. This figure may then be considered as the valence or potency value for this material. The dog is a biologic instrument difficult to standardize and, therefore, variations, occasionally wide and difficult to interpret, do occur. It is remarkable, consequently, that Weech and his associates,[157-161] employing a wholly dissimilar technique to study the effect of diet on plasma protein formation, obtained strikingly corroborative results. In Table I it can be noted that beef serum or dried beef serum is superior to several food materials. Other substances possess progressively more limited capacities to induce protein regeneration. Lactalbumin, egg white, and casein exhibit an average ability, while gelatin, pancreas, and zein (protein of corn) are poorest. The assay values obtained by Weech and associates (of Johns Hopkins, Columbia, and Cincinnati Universities) are in substantial agreement for these same foods. The discrepancy between the findings of the former two groups of investigators and those

shown for Melnick, Cowgill, and Burack[162-165] is probably related to the adoption of assumptions in the experimental methods later found to be untenable, or to differences in experimental methods.

TABLE I. THE POTENCIES OF VARIOUS FOOD PROTEINS IN FORMING BLOOD PLASMA PROTEIN*

REFERENCE	HIGH POTENCY	MEDIUM POTENCY	LOW POTENCY
Rochester (Whipple and associates)	Serum, beef, 38† Serum, beef, dried, 28	Salmon bread, 24† Yeast, fresh, autoclaved, 23 Bran flakes, 23 Kidney, pork, cooked, 22 Liver, pork, raw, 17-33 Kidney, pork, cooked, 19 Rice polishings, 19 Gizzard, 19 Thyroid, powdered, 19 Rice, polished, 19 Lactalbumin, 18 Skeletal muscle, beef, 18 Egg white, 17 Irish potato, powdered, 16 Salmon, 16 Liver pork, raw or cooked, 15 Soy bean, 14, 8 Heart, beef, 13 Casein, 12 Liver extract, 12	Spleen, 10† Red blood cells, dog, 10 Brain, pork, 8 Stomach, beef, 7 Salmon, canned, 7 Gelatin, 2, 9 Pancreas, 6 Kidney, pork, cooked, 6 Zein, 0
Columbia (Weech and associates)	Serum, beef, 0.801‡	Egg white, 0.613 Beef chuck, 0.475 Beef liver, 0.436 Casein, 0.388	Gelatin, –0.093
Yale (Cowgill and associates)	Serum, protein, beef, 0.53 Casein, 0.45 Lactalbumin, 0.38		

*From Madden, S. C., and Whipple, G. H.: Plasma Proteins: Their Source, Production and Utilization, Physiol. Rev. 20: 199, 1940.

†Figures mean grams of new plasma protein resulting from feeding of 100 Gm. test protein.

‡Ratios are expressions of relative effectiveness.

ANALYSIS OF FACTORS INFLUENCING SELECTION OF SUBSTANCES FOR DIETS DESIGNED TO PROMOTE PROTEIN SYNTHESIS

Table I with each food substance labeled numerically, according to its capacity to correct hypoproteinemia, should, therefore, serve as a guide in the development of diets aimed at treating this condition in man. Selections from this chart must, however, satisfy criteria other than mere effectiveness in protein regeneration. For instance, beef serum for oral use, unless pasteurized, would be dangerous since the recipient might acquire clinical brucellosis by this means. If pasteurized, the objection remains that the bulk of liquid looms large for the total protein available, that is, but 50 to 60 Gm. per liter is the most that can be anticipated. Dried beef serum is available on the market as "light blood albumin." This material, used commercially in the preparation of a coating for leather and textiles, and in the manufacture of water-resistant glue for veneering purposes, is soluble to at least 100 Gm. per liter of water and may be used as such, or the protein may be carried down as a protein curd by boiling. Decanting the supernatant liquid leaves the residual coagu-

lum which is about 13 to 15 per cent protein. Weech[161] has stated that it does possess a "lingering unpleasant taste, difficult to disguise and rendering it rather unpalatable for human consumption." The associated odor is reminiscent of the hot glues used in woodworking and cabinetmaking. With the exception of a product made available to us for experimental purposes, crystalline bovine plasma protein, about 95 per cent protein, we are, therefore, relegated to items of lesser (medium according to the table) potency. Many here can be excluded by objections which appear to be reasonable. All uncooked meat is eliminated for routine use because of the danger of transmitting brucellosis.[166] There seems to be no simple manner of excluding this possibility from uncooked flesh short of pasteurization. Culture methods require too prolonged periods of incubation and are impractical for excluding positively this possibility. The use of cooked kidney yields erratic results (note columns 2 and 3 of Table I). The ingestion of yeast and bran in bulk tend to cause a diarrhea in many individuals. Thyroid powder and liver extract are obviously unsuited for quantity usage. Gizzard, beef muscle, and salmon allow little variety in the menu and the per cent of protein in each gram bulk, is large. The fat content of soy bean meal is too high. Lactalbumin, casein, egg white (ovalbumin and ovaglobulin), polished rice, and powdered Irish potatoes ultimately remain for consideration. We have acquired no experience with the use of the latter two substances. The first three substances are complete proteins (contain all the essential amino acids) and have been the materials used in acquiring much of our biologic information. They are cheap, particularly the casein and lactalbumin, are available in quantity, can be easily added to any one of several dietary dispensing vehicles, and, for the average palate, present no serious degree of gustatory repugnance. The selection of casein and lactalbumin for fortifying diets was favorably influenced also by the apparently high-grade protection of the liver obtained with feeding of this substance in the experiments of Davis and Whipple.* Skim milk powder was, therefore, selected as the stock material since it fulfilled so many of the requirements. The cost per pound is very reasonable (approximately 20 cents per pound); many billions of pounds are produced annually. In producing skim milk powder, nothing is added to the milk and only the butterfat, water, and much of the vitamin content is removed. The average composition of skim milk powder is as follows:[167]

COMPONENTS	PER CENT
Fat	1.0
Water	3.0
Protein	37.8
Casein circa	32.0
Lactalbumin circa	5.2
Lactoglobulin circa	0.5
Lactose	49.7
Ash	8.5

*In this connection it seems pertinent to note that casein and lactalbumin have a significantly higher methionine content[234] (3 and 2.8 per cent, respectively) than several other edible proteins. Hen ovalbumin, also an integral part of the diets, probably has the highest methionine content with 5.3 per cent.

The total nitrogen composition of skim milk powder is about 5.4 per cent. Of this total nitrogen, 76 per cent is casein nitrogen, 18 per cent noncasein protein nitrogen, and 6 per cent nonprotein nitrogen. This material* and a fortifying substance to augment the carbohydrate content were the selections then for diets to be devised which would possess a high protein, carbohydrate, caloric, low fat composition. In developing this theme it seemed wiser to use as vehicles fruit juices,† eggnogs, purées, and soups, whose nutritional makeup could be augmented with protein and carbohydrate. Lactose was originally chosen to enhance the carbohydrate content since there was evidence in the literature suggesting that it was less liable to induce diarrhea when fed in quantity than were other sugars. This finding has not been confirmed, and it is our impression that this problem is minimal whenever the dispensing apparatus is maintained thoroughly clean or preferably sterilized. An additional aid in avoiding this difficulty is the routine use of some form of appropriate refrigeration for those portions of the diet awaiting dispensing. Should diarrhea develop it can usually be remedied satisfactorily and promptly by rechecking on the techniques involved in the aforementioned precautions, and by the coincidental administration of paregoric in modest amounts. For intervals of several months no single instance of diarrhea will appear, despite a frequent change in personnel among the nursing staff and semiskilled help preparing this material, under the supervision of the dietetic staff. Finally, we have been compelled to abandon the routine use of lactose because of lack of availability of the material, and because its cost was so great compared to beet or cane sugar. Due to the strictures involved in securing sufficient quantities of this carbohydrate we have been substituting "cerelose."‡ It has proved a satisfactory, inexpensive replacement for the cane or beet product, and has the added advantage of being only three-fourths as sweet as sucrose.

The diets with which we have been concerned have been almost exclusively liquid in nature. This has had advantages and disadvantages. Against the idea is the fact that only a relatively meager selection and rather unvaried menu is available. Also, it is a common feeling that no meal is really eaten, certainly not a satisfying one, unless some article can actually be chewed on during the course of the repast. Unfortunately for this frame of mind, clinical experience has shown that the individual's insistence on swallowing a partially masticated bolus of solid material, a piece of beefsteak, for example, presents to the somewhat occluded gastroduodenal aperture a well-nigh insoluble problem in aboral transportation. A short period of time spent in explanation with such individuals, invariably removes this reluctance to co-

*A variety of more refined commercial preparations have been sampled as alternative means of augmenting the protein and carbohydrate values. These possess certain advantages of increased palatability and solubility, but have been so disproportionately expensive as to discourage their routine use and rather limit the application to special instances.

†A host of carriers has proved satisfactory for this purpose, and a partial list would include orange juice, lemonade, pineapple juice, apple cider, cherry nectar, bananas powdered or homogenized from the whole fruit, grape and grape fruit juice. Substituting freely from this list will alter the over-all content of protein, carbohydrate, and fat very little since the preponderant influence on these nutrients comes from the fortifying substances of milk powder and a sugar.

‡Dextrose from corn processed by the Corn Products Refining Company, St. Paul, Minn.

operate during the temporary all-liquid feeding regimen. The fluid character of the diets has proved advantageous to the dietetic staff. Semi- or unskilled workers readily learn the simple necessary manipulations and mechanics involved in the production of these formulas. On the practical side it was essential that one diet be available for drip feeding through even a small bore nasal tube.

A number of diets have been proposed in the literature for purposes of alimentation via the oral, gastrostomy, or jejunostomy route. In each instance they have not been adapted to this study because of one or more of the following objections:

1. The percentage of fat contained was too high. The inadvisability of this has been mentioned earlier.

2. The protein percentage was too low. Such diets would be automatically excluded.

3. The number of calories per cubic centimeter, described by the neologism, calorie equivalent, is too small. If attention is not devoted to this detail, the bulk of liquid administered becomes excessive as one strives to attain a high caloric feeding schedule. About 1.5 calories per cubic centimeter is desired.

In recapitulation it can be said that the contemplated diet was to possess these characteristics: It would be a high protein, carbohydrate, low fat diet with a high caloric equivalent; its production would be simple, relatively inexpensive, and in a form readily tolerable, in appearance and taste to the patient—and to his intestinal tract. No emphasis was to be placed on the vitamin content of the diet and it was decided to rely on the routine administration of such quantities of vitamin B_1 (thiamine), B complex (crude liver extract), C (ascorbic acid), and K as appeared indicated in each individual case. The minerals, calcium, phosphorus, and iron have been estimated to be present in satisfactory quantities when a single portion of Diet I or II is consumed.

This information was secured chiefly from charts in Bowes and Church[235] and the values listed here have been reduced to close approximations.

	DIET I (ONE PORTION)	DIET II (1,500 C.C.)
Calcium	5.2 Gm.	2.8 Gm.
Phosphorus	4.2 Gm.	2.6 Gm.
Iron	19.0 mg.	16.0 gm.

These amounts listed exceed, when but a single portion of either diet is consumed, the daily allowances recommended in the *Handbook of Nutrition* for 1943.

DESCRIPTION OF PROPOSED DIETS

For the preoperative dietary management of surgical patients, Diets I, II, IIA, III, and IV have been developed. In each the goal was to adhere as closely as possible to the previously listed qualities and characteristics. Specific differences, within these limitations, were "built into" each diet. Diet I is designed to be quite reasonably palatable, with a wider range of vehicles, and

DIET I

	Calories		2,426.00			
	Protein		160.20 Gm.			
	Fat		18.05 Gm.			
	Carbohydrates		407.00 Gm.			
	Caloric equivalent		1.60			
		VOLUME OR WEIGHT	P.	F.	CHO	CALORIES
7 A.M.	¼ cup oatmeal, strained	10 Gm.	1.4	0.75	6.8	40
	¾ cup skimmed milk	180 c.c.	6.3	0.40	9.0	65
	2 tbs. lactose*	30 Gm.			30.0	120
9 A.M.	1 cup orange juice	240 c.c.			24.0	96
	1 tbs. lactose	15 Gm.			15.0	60
10 A.M.	Skimmed milk powder	120 Gm.	40.4	1.20	58.8	408
	1 cup skimmed milk, warm	240 c.c.	8.4	0.50	12.0	86
	½ cup puréed peas	50 Gm.	3.3	0.20	10.1	55
12 M.	1 cup orange juice	240 c.c.			24.0	96
	1 tbs. lactose	15 Gm.			15.0	60
2 P.M.	Eggnog:					
	1 egg	Variable	6.4	5.80	0.4	79
	Skimmed milk powder	30 Gm.	10.1	0.30	14.7	102
	1 tbs. lactose	15 Gm.			15.0	60
	1 cup skimmed milk	240 c.c.	8.4	0.50	12.0	86
4 P.M.	Skimmed milk powder	120 Gm.	40.4	1.20	58.8	408
	1 cup skimmed milk, warm	240 c.c.	8.4	0.50	12.0	86
	¼ cup puréed beans, string (fresh, frozen, or canned)	50 Gm.	1.0	0.10	3.3	18
6 P.M.	1 glass grape juice	240 c.c.	0.8		44.0	179
8 P.M.	Eggnog, same as 2 P.M. feeding	about	24.9	6.60	42.1	327
	Totals	1,500 c.c.	160.2	18.05	407.0	2,431

*Beet, cane sugar, or cerelose can be substituted.

to be presented to the patient in divided portions every few hours during the daytime. In Diet II, with a high caloric equivalent, the emphasis is less on tastiness, yet it should be palatable, and more on securing a freely flowing mixture, to facilitate feedings via a nasal tube. Diet IIA consists of 1,000 c.c. of Diet II to which has been added the filtered residue remaining from one pound of ground raw liver after homogenization in a Waring blender. This machine effects nicely the breakdown of liver parenchyma into finely divided particles capable of passing easily through a nasal tube when they are suspended in Diet II as the vehicle. The fibrous connective tissue elements resist

DIET II

Carbohydrates		408.8 Gm.	
Protein		120.4 Gm.	
Fat		37.2 Gm.	
Calories		2,446.0	
Volume		about 1,500.0 c.c.	
Caloric equivalent		about 1.6	
	CHO	P.	F.
6 whole eggs		36.0	36.0
2 egg whites		8.0	
4 oz. skimmed milk powder	58.8	40.4	1.2
300 Gm. lactose*	300.0		
1,000 Gm. skim milk	50.0	36.0	
5 gr. salt (may be added when indicated)	408.8	120.4	37.2

*Beet, cane sugar, or cerelose can be substituted.

DIET III

THE DAILY DIET IS SELECTED FROM THESE ITEMS:

1. Orange juice (strained through fine wire strainer or double thickness of cheesecloth)
2. Fruit juice (strained) in same manner as orange juice
3. Malted milk, eggnog, cocoa made with skim milk
4. Cottage cheese
5. Junket, custard, jello, tapioca, cream, rice custard made with skim milk
6. Eggs (soft cooked, poached, coddled, scrambled in a double boiler without fat)
7. Thoroughly cooked cream of wheat, farina, or rice
8. Chicken or beef broth
9. Strained tomato juice
10. Boiled skim milk
11. Arrowroot cookies

THESE ITEMS ARE OMITTED FROM THE DAILY DIET:

1. Coarse cereals
2. Fruits
3. Vegetables
4. Meat
5. Potatoes
6. Raw milk
7. Bread or toast
8. Fried foods, pastries, rich desserts
9. Condiments, spices, vinegar, meat sauces, etc.
10. Alcoholic beverages
11. Cream, butter, fatty foods

this fractionating process successfully, however, and must be filtered out by passage through several folds of surgical gauze. This can be accomplished before or after a partial dilution has been attained but adds to the tedium of preparation and, therefore, limits the output. Also, it is not a preparation easily consumed by the mouth, and there is, in a substantial percentage of cases, even an intolerance for the diet after it has been instilled by gavage. Diet III is a nonresidue diet. Its use has been abandoned after a brief experience indicated that it possessed practically no specific benefits, while disadvantageously limiting seriously the caloric and protein intake. Diet IV contains 100 Gm. of powdered bovine plasma protein in 1,000 c.c. of tap water or some tastier vehicle. We have sampled the potentialities of this diet. It was felt that by complementing the diet with such a pure protein with so high a potential capacity to induce plasma protein regeneration, a pyramiding of benefits might be effected. Our observations have substantiated this thesis and will be dealt with in the case reports.

THERAPEUTIC APPLICATION OF PROPOSED DIETS

These diets, particularly I and II, have played an integral role in the nutritional preparation of patients with several varieties of surgical conditions. They have been employed successfully for this purpose in cases of

DIET IV

Carbohydrates	0 Gm.
Protein	95 Gm.
Fat	0 Gm.
Calories	380 approximately

	AMT.	CHO	P.	F.
Tap water*	800 c.c.	0	0	0
Powdered bovine plasma protein	100 Gm.	0	95	0

*Other vehicles can be used to suit flavor or taste.

hyperthyroidism, biliary tract disease, whether due to stone, stricture, or carcinoma, old burns, bronchiectasis, chronic empyemas, osteomyelitis, and, any process surgically remediable, when recent marked weight loss is known to have occurred, and especially in patients with ulcerative disease of the stomach or duodenum, carcinoma of the esophagus, stomach, duodenum, colon, or rectum. It is with the surgical diseases of the gastrointestinal tract that the broadest orientation has been achieved. On the basis of experience acquired during the supervision of the nutritional care of more than 200 patients with ulcer of the stomach or duodenum, in excess of 100 with cancer of the stomach, and nearly as many instances of neoplasm of the colon and rectum, the following observations and conclusions have been made. The validity of such therapeutic contentions as follow have been tested practically, in repeated instances, upon patients on an active gastroenterologic surgical service and, if proved true, only then accepted as the current procedure. Now, admittedly, broad gaps, which do not permit categoric pronouncements are yet present in our knowledge; but in general, almost any case of gastric carcinoma or gastric or duodenal ulcer can be segregated into one of the following categories for the appropriate therapeutic care.

Ulcerative or Neoplastic Lesions of Stomach and Duodenum

Patients Exhibiting Little or No Pyloric Obstruction.—Patients with little or no pyloric obstruction receive Diet I by day and Diet II by night. The diets are furnished ad libitum in freshly prepared portions ample enough to provide the 5,000 to 6,000 calories these individuals are urged to consume daily. Intakes far in excess of this figure as a rule generally are attained and well tolerated. Commonly individuals have averaged 7,000 to 8,000 calories per diem for two or more weeks. A few patients have accepted 10,000 calories in a single day without detectable untoward effects. Those persons drinking a quantity of the first diet during the waking hours, sufficient to provide about 5,000 calories, are not customarily given Diet II. For totals lower than this, however, the individual is urged to drink a midnight supplement of Diet II, or it is readily instilled by the nasal tube. Alimentary glycosuria was rather anticipated, particularly, since many of the patients on the service were elderly. Qualitative twenty-four hour urine glucose determinations upon more than two dozen, otherwise unselected, nondiabetics, receiving an average of 5,000 to 6,000 calories daily, indicated but a single instance of glycosuria. This was a 1 plus reaction. The usual practice is to weigh these patients daily or several times a week. Yet weight gain, in the absence of dehydration, after days of abundant eating and without diarrhea, is often quite astonishingly small. This has been difficult to interpret. A few "basal" metabolism studies upon these patients after just such a period of plentiful caloric intake, have not demonstrated convincingly that an abnormally increased metabolism exists. The inconclusiveness of this is apparent to anyone realizing the fiction connoted by the term basal metabolic rate for any person capable of physical or emotional activity. Protein, with its high specific dynamic action, present as it is in

large quantities, may influence the total amount of substance ultimately to be stored in body depots. Also, occult edema, which could represent as much as 5 to 6 per cent of the total body weight might be present but undetected. The simultaneous substitution with bodily tissue and disappearance of this amount of fluid by virtue of the improved nutrition is a tentative possible alternative explanation. Finally, any conversion of protein or carbohydrate to fat would require an intake to storage ratio of more than two to one. In order to exclude the rather unlikely possibility of a failure of intestinal absorption of protein and carbohydrate, samples from four-day stool specimens were analyzed. These determinations uniformly indicated excellent absorption of the protein component despite an intake of as much as 500 Gm. daily. Consistently, there was less than 10 per cent of the ingested protein in the stool.

Cases 3 and 4 represent rather typical examples of this type of feeding plan.

CASE 3 (No. 741769).—A. W., aged 59 years, reported that for fifteen months prior to admission there had been epigastric postprandial distress associated with nausea, vomiting, and a developing weakness. Emesis had increased gradually in frequency. Weight loss had been steady and more marked recently, so at the time of admission the weight loss was 30 per cent. No obstruction was noted in a gastrointestinal series of roentgenograms interpreted as showing a large gastric ulcer. During the following twenty-one days this patient received an average of 6,000 calories daily, from Diets I and II ad libitum. The patient displayed no diarrhea nor glycosuria, and had no gastric retention or emesis. This represented an intake of more than 7,200 Gm. of protein or nearly 350 Gm. daily. One transfusion of 350 c.c. of blood was given. No dehydration or edema was present on admission, nor did any develop during this period. The hemoglobin, red blood cell, and plasma protein values are listed below:

DATE	3/29/44	4/18/44 (DIETARY PREPARATION STARTED)	4/24/44	4/28/44	5/1/44	5/6/44	5/8/44 (DAY OF SURGERY)
Hemoglobin (Gm. %)	9.45	8.46	11.8		10.3		
R.B.C. (millions per c.mm.)		2.55			3.26		
Plasma proteins (Gm. %)	3.72	5.7		5.6	6.2	5.4	

It is not too difficult to explain how such large amounts of protein in the diet seemingly fail to evoke by this means a consistent detectable increase in the plasma protein values. This is, I believe, a clear manifestation of how unsatisfying may be the information secured through determinations of the plasma protein value. Often, small changes in these values appear to be associated with quantitatively much larger alterations in the plasma volume and the labile protein stores or components of bodily tissues; for these three quantities, albeit regulated by a host of external and internal factors, appear to remain in equilibrium. Considered somewhat differently they represent the three geometric dimensions required for the definition of volume. The first two of these determinations, plasma proteins and plasma volume, usually can be secured readily, but the final dimension, the tissue component, seems at this writing least susceptible of mensuration. When, however, a clear-cut rise or fall in the plasma protein value is noted, judgments as to the state of nitrogen balance can be

offered with more assurance of their accuracy. Yet, even here, the incompleteness of these observations hovers like a discouraging shadow over any illuminating discussion of the problem. It seems logical to infer that one of the mechanisms producing the hypoproteinemia originally could be capable of maintaining this status quo, despite the provision for ample sources of protein for regeneration. Subjectively this patient was much improved and appeared adequately prepared nutritionally for surgery. No detectable evidence of hepatic dysfunction existed. The postoperative convalescence was prompt and complicationless.

CASE 4 (No. 732161).—C. B., aged 68 years, had noticed epigastric distress of a mild sort for two years before admission. For the last year there had been anorexia and a progressive weight loss which at the time of admission equaled thirty-five pounds, about 27 per cent of the usual body weight. The local physician had informed her that she was anemic and had a tumor of the stomach. These diagnoses were confirmed, and x-ray studies secured in this clinic revealed a massive carcinoma involving the distal two-thirds of the stomach. These pictures corresponded well with the size of an easily palpable epigastric mass. Gastric retention was not present. Three transfusions adjusted the hemoglobin satisfactorily. This patient averaged in excess of 6,000 calories daily for thirteen days from Diets I and II, without demonstrable weight gain. After this preparation she was operated upon and about a 96 to 98 per cent gastric resection completed. Convalescence was uneventful and the patient was discharged on the twelfth postoperative day.

Cases Exhibiting Pyloric Obstruction, But Less Than Complete in Degree.—Patients with partial obstruction are given limited quantities of Diet I by day and Diet II by night. From midnight to 8:00 A.M., during the initial days of this feeding schedule, no more feeding is allowed. The stomach is then evacuated by nasal tube and the quantity removed is accurately measured and recorded. Patients having aspirations of less than 300 to 500 c.c. are continued upon this regimen with a limited intake when the calorie intake approximates or exceeds 3,500 calories daily. For example, if the intake consisted of one portion of Diets I and II with 500 c.c. being aspirated, the total effectual nutrient intake would substantially surpass the minimum requirement of 3,500 calories. Those patients, in this category, with high-grade but not complete pyloric obstruction, in whom the retention is more voluminous, are cared for in the following fashion: A nine-hole nasal tube is inserted into the stomach and the Diet II mixture allowed to trickle at a very slow rate, drop by drop, through a Murphy drip set. A demonstration of this setup is portrayed in Fig. 5.

For this purpose it has proved advantageous to use intravenous flasks* so constructed that air rises through the contents in the container while the liquid flows from another dependent aperture. This bubbling effect provides enough mild agitation to prevent much of the aggravating tendency for plugging which occurred when certain other types of dispensers were employed. The average patient readily cooperates in regulating the flow rate by adjusting, from time to time, a thumbscrew clamp fastened distal to the Murphy drip bulb, which serves as a visible and reliable guide during waking hours. Maintenance of such equipment in smooth working order is but another of the many burdens a tolerant nursing staff discharges so faithfully with but scant recog-

*Manufactured by The Upjohn Company, Kalamazoo, Mich.

nition. Occasionally the prolonged presence of an indwelling nasal tube brings about real torment through local irritation. Two devices have been tried, with the second the more satisfactory in our experience. Woldman[168] suggested the use of a collapsible indwelling nasal tube. This device closely resembles Penrose tubing about ¼ inch in width with a spiral strand of silkworm gut threaded down the middle to serve as an obturator. This facilitates passage of the tube into the gastric area. In the absence of the manufactured article, ordinary narrow Penrose tubing can be passed, with the aid of a catheter, through the nose and out the mouth. Then a large size gelatin capsule can be tied to a short catgut leader fixed to the aboral end of the tube. When this bolus is swallowed

Fig. 5.—Drip feeding apparatus.

with a gulp of liquid or spoonful of mashed potatoes, the tubing is readily led along down the esophagus. The soft compressible rubber cylinder is readily tolerated by individuals aggravated by a stiffer conduit. It does have an annoying inclination, because of this excessive flexibility, to kink and thus plug, with changes in head posture by the patient. The alternative device has been the use of a vinylite resin (vinyl acetate) tube, of small bore. This material is smooth, pliant, and lightweight. It glides easily over mucous membranes and evokes little adverse criticism. The lack of an abundant supply plus a tendency to deterioration after prolonged exposure to gastric acids has limited its application to the more sensitive individuals. It has seemed to be a useful and satisfactory expedient.

As ancillary measures in the treatment of this type of case, we have routinely administered atropine sulfate, gr. 1/150, and sodium phenobarbital, gr. 1 to 2 hypodermically, every four to six hours. Mears[169] has pointed out that therapeutic doses of atropine sulfate, hypodermically, every few hours materially reduces the quantity of gastric juice secreted; Merendino and Litow[170] noted a similar, although less marked, depression on the flow of gastric juice when sodium phenobarbital was injected periodically subcutaneously. In addition, the sodium phenobarbital aids in controlling the motor restlessness and irritability often encountered in such cases where ulcer is the underlying mechanism. Also, it allays in a large measure the discomfort from an ordinary nasal tube. These various adjuvants, we feel, reduce the total bulk of fluid seeking outlet through a gastroduodenal opening reduced in lumen and thereby contribute to an adjustment to tolerable limits, the task of a decompensated stomach.

An additional physiologic consideration is worthy of discussion at this time. In certain instances patients being treated by the Sippy regimen were noted to exhibit large volumes of gastric retention unvaryingly day after day. Then, after the employment of the intragastric drip feeding routine with Diet II, the retention frequently decreased significantly in amount and not infrequently disappeared completely. This phenomenon, it is granted, is open to alternative explanations, yet it provides interesting material for speculation. To prescribe the Sippy regimen is to prescribe a high fat type of feeding. One of the most clearly established physiologic responses noted after a fatty meal is an inhibition of gastric motility.[171-175] This depression of peristaltic activity conceivably depresses gastric evacuation and, under such circumstances, is therefore not acceptable. Also, in the Sippy method of treating ulcers, the patient customarily gulps a two or three ounce mixture approximately every hour or so. The swallow carries down with it a complement of air and then this quantity is presented before the narrowed pyloroduodenal exit. In our experience, the stomach more efficiently evacuates its contents when called upon to handle a cubic centimeter every minute than when it must adjust for a 60-90 c.c. load, all at once, repeated hourly.

A patient treated in this fashion is reported in Case 5. The stability of the blood pressure and pulse rate and the smooth brief period required for convalescence seem significant in this man with a serious weight loss.

CASE 5 (No. 728192).—W. W., aged 61 years, had chronic epigastric distress and anorexia for the three years prior to admission. During the final three months of this period these symptoms had increased in severity and there was an associated nausea, vomiting, and ease of fatigability. During this latter interval, he had lost thirty-four pounds in weight, a 30 per cent weight loss. The x-ray examination of the stomach indicated a "marked retention of barium and findings which would be most consistent with an ulcerating carcinoma of the antrum." During a four-week period, preparation was secured largely with intragastric feedings of Diet II supplemented with plasma transfusions and 20 per cent glucose intravenously. This preparation was complicated, prolonged, and made less satisfactory by periodic episodes of almost complete gastric retention which would spontaneously clear up with continuation of the same therapy under which they had developed. There was a 1.5 kilogram weight increase and the plasma proteins fell from 7.5 to 6.7 Gm. per cent during the period of preparation. At the conclusion of this preparation

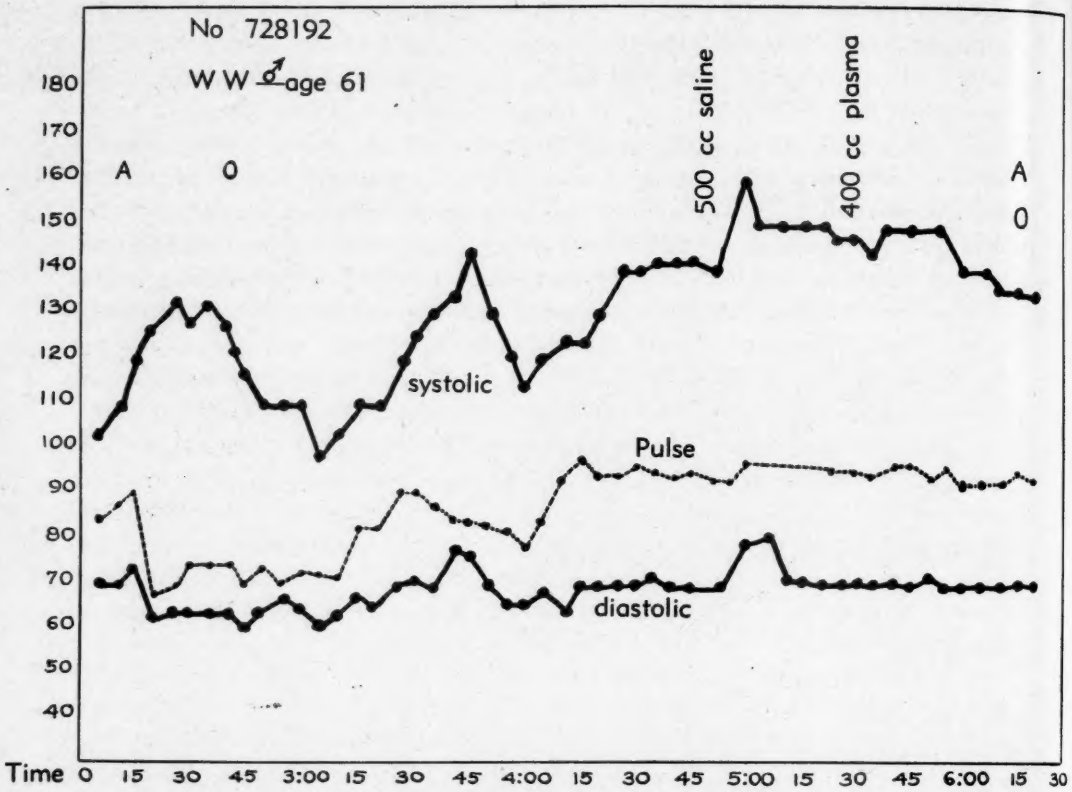


Fig. 6.—Record of blood pressure, pulse, and intravenous fluids during anesthesia. Note stable blood pressure and pulse rate after initial early anesthesia effects (Case 5).

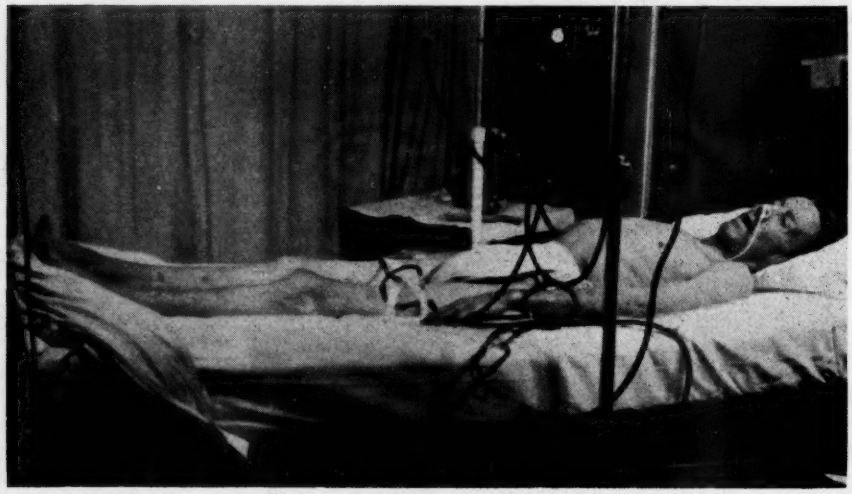


Fig. 7.—Photograph of patient during preparation (Case 5).

a subtotal gastric resection was performed and convalescence was uneventful, with the patient leaving the hospital on the fourteenth postoperative day. This patient has remained well during the past one and one-half years since surgery and returned to a more normal weight.

Cases With Complete Pyloric Obstruction.—In instances of complete obstruction, two alternatives are present. A jejunostomy can be made for feeding purposes, and the surgery of magnitude performed when an adequate nutritional state has been restored. We have had virtually no experience with such a plan. Apparently, however, even such a minor procedure can be associated with the development of a temporary but rather intractable state of negative nitrogen balance. Cuthbertson[225-227] first called attention to the increased rate of nitrogen elimination in the urine after injuries (fractures), found the imbalance rose sharply in the three days after trauma, and persisted for several more days, despite, and almost uninfluenced by, substantial augmentation of both the caloric and nitrogen intake. Howard and his associates[229, 230] have corroborated these observations and have protracted the investigation while noting the maintenance of a negative nitrogen balance for more than one month in certain fracture cases. In the simpler operative procedures the nitrogen loss is as real but shorter in duration and quantitatively smaller. Peters[231] reported that a similar situation occurs in the acute infectious processes studied, with a daily nitrogen deficit persisting after subsidence of the acute aspects of the disease, despite an intake of 178 Gm. of protein per day. This seemingly anomalous transitory failure of the bodily mechanisms to anabolize available amino acid elements has been interpreted by Albright[232] as an expression of Selye's "alarm reaction" engendered by an abnormal secretion of adrenal cortical hormone "S." The solution to this particular conundrum of biology may well involve mechanisms more intricate than this, however, for Munro and Cuthbertson[228] noted the absence of any real antianabolic period when rats were deprived of protein for a sufficiently long period prior to a fracture injury. Also, Co Tui and collaborators[233] were able to develop a strongly positive nitrogen balance in patients submitted to major surgical procedures when about 200 Gm. of protein (the powdered enzymatic digest of casein and pork pancreas, Amigen) was ingested daily beginning in the early phases of postoperative recovery. Elman and associates,[179] too, approximated these results postoperatively utilizing the same source of protein. Within the scope of our present knowledge it is difficult to resolve these apparent contradictions between the groups of investigators. However, the impression is created that whenever feasible the ingestion of protein as an aspect of preoperative preparation is as effective as, or more effective than, corresponding increments made available to the patient in the post-traumatic interval.

The other choice is to supply the patients nutritional needs largely or completely by the intravenous, subcutaneous, or sternal routes as best one can, and this is often accomplished with modest effectiveness. Periodically, reasonable quantities of Diet II are supplied and then followed by a fasting interval. The gastric aspiration at that time is checked for any relenting in the obstruc-

tive element. The caloric intake is thereby complemented somewhat. The bulk of the daily caloric intake is provided, nevertheless, by hypertonic glucose solutions, preferably 20 per cent in distilled water, dripped intravenously at the rate of 100 to 125 c.c. per hour through a fine caliber (No. 20 or 22 gauge) needle. It should require ten to twelve hours for 1,500 c.c. (yielding 1,200 calories) to be injected. Hourly rates in excess of this encourage glycosuria with subsequent loss of greater amounts of the nutrient and a concomitant undesirable dehydration effect. When it is injected at this suggested pace, which exceeds somewhat the prescribed "desirable rate of infusion,"[224] the total spillage in the twenty-four hour urine collection in our experience has been consistently less than 1 per cent. Insulin is not added to the solution in the normal subject, and evidence of the beneficial effects of its use under such condition is controversial.[176-178] The use of a cubital vein with the arm hyperextended in the routine manner for intravenous therapy is to be avoided because of several considerations. This position is acutely distressing for anyone to maintain longer than a short while. Consequently, the patient tries to relieve the discomfort by some degree of flexion at the elbow, readily and frequently plunging the needle through the back wall of the vein and leading to a paravenous infusion. With strongly hypertonic solutions this is a particularly undesirable complication, and, at best, results in a locally tender, inflamed sore arm. Another reason to avoid this site is related to the frequent occurrence of thromboses in veins carrying hypertonic glucose solutions. If the broader channels are occluded early in the course of a prolonged feeding schedule, the difficulty of the task is enhanced and these areas are no longer readily available for any emergency infusions of blood or plasma that may be required during the operations or the convalescence. The preference has been, therefore, to insert the needle into a forearm vein, away from the cubital fossa, and in such a position as to allow the arm a free range of motion. (see Fig. 8).

No arm board is required. A feeling of assurance is imparted the patient by splinting the forearm slightly with a few thicknesses of newspaper or cardboard encircling the area and fixed in place by a strip of bandage. The caloric intake is further supplemented by the subcutaneous administration of at least 1,000 c.c. of 5 to 10 per cent glucose in distilled water or saline solution as determined by the electrolyte need and hydration of the patient. A positive nitrogen balance is strived for by two means. Protein is provided by the daily intravenous administration of liberal amounts of plasma. Nitrogen equilibrium in dogs[142, 149, 156, 180, 181] and man[182] can be maintained for many days in this fashion, excellent evidence that such parenterally administered protein is metabolized. It is soon noted under such conditions that surprisingly larger quantities of plasma must be infused than one would calculate from the theoretical plasma volume, to elevate appreciably the plasma protein value. Since protein so injected does not cause a disproportionate rise in urinary nitrogen, this is then explicable as another manifestation of the extremely fluid equilibrium which exists between plasma protein and other protein stores. The conclusion is equally reasonable that small deficits in the former mirror quanti-

tatively gross debits in the latter. Earlier workers[148, 160, 163] noted that of the total nitrogen lost during fasting, only a small fraction could be accounted for on the basis of the albumin lost from plasma protein. Sachar, Horwitz, and Elman[183] studied the problem in some detail in dogs and arrived at a ratio of 25 to 30:1 for the respective contributions of albumin and tissue protein to total amount lost during a fast. The evidence[184] on the same subject for man is meager but in general agreement with the ratio revised toward 30 to 40:1. A few simple calculations may serve to clarify this point. If, in a 60 kilogram man, the plasma protein value has been lowered by starvation from the normal average 7.5 to 6.5, this represents but 30 Gm. of protein lost from the plasma volume of this individual.* Granted the tissue-plasma protein ratio of at least

Fig. 8.—Suggested position of needle for prolonged intravenous therapy.

30:1 exists, then 900 Gm. of tissue protein have also been lost. To replace this, therefore, about 12,400 c.c. of plasma with total proteins of 7.5 Gm. per cent are required. The total eventually necessary, however, surpasses even this figure, since such an amount cannot be given intravenously within even a few days. During this interval additional protein is being catabolized which needs to be replaced by more plasma. A good deal less than complete replacement therapy is, therefore, the only goal actually attainable. The surgeon should appreciate the difficulty of restoring intravenously completely the body protein depots, aim at preventing additional depletion of existing protein stores, and, if possible, establish a nitrogen balance as favorable as possible. Fortunately in this situation there is a true equilibrium, and in the situation where ample stores exist, the protein reservoirs are capable of replacing 40 to 60 per

*$\frac{\text{(Aver. plasma prot. \%} - \text{reduced value)}}{7.5 - 6.5} \times \frac{\text{(Wt. in kg.)}}{60x} \times \frac{\text{(\% total body wt. in plasma)}}{.05} \times 10 = 30$ Gm. protein

cent of the total circulating plasma proteins in twelve hours after a sudden severe loss. Over a longer interval with repeated demands, these depots may supply an amount of protein equal to 200 to 300 per cent of the original total circulating plasma protein. This mechanism appears to function in man[185] at a reduced rate if the protein depletion has been associated with the production of shock.[186]

A portion of the nitrogen requirements can be provided through the agency of intravenously injected amino acids, usually obtained from the enzymatic or acid hydrolysis of casein. The resulting mixture in the latter instance is poor in tryptophane and probably also the sulfur-containing amino acids and these essential amino acids must, therefore, be replaced if the solution is to be effective in protein regeneration. After the original experiments of Lowei[187] in 1901 had demonstrated that, by feeding protein digests nitrogen equilibrium could be attained, observations on parenteral alimentation with such amino acid preparations were for many years sporadic. Abderhalden, Frank, and Schittenhelm[188] and Abderhalden[189] tried rectal administration and found evidence of absorption and utilization. This has been confirmed since.[190] Henriques and Andersen[191] kept a goat in positive nitrogen balance for one month with intravenous injections of meat digests. To Elman belongs the credit for reviving and stimulating interest in this problem. Much of our present knowledge and success the method now enjoys is related to the efforts of him and his associates.[192-198] They have demonstrated the necessity of having mixtures containing all the essential amino acids, if retention and protein synthesis is to be accomplished. In dogs a positive nitrogen balance has been effected with intravenous injections of amino acids as the sole source of protein. It has even been possible to induce some degree of plasma regeneration under these conditions[200] or when the ten essential amino acids (Rose) are provided in pure crystalline form.[199] Investigators[201-204] have had difficulty in acquiring unequivocal evidence that plasma protein regeneration can be realized in adults by the infusion of amino acids as the sole source of protein. Mueller, Fickas, and Cox[205] using an enzymatic hydrolysate of casein, 85 per cent, and pork pancreas, 15 per cent, found that 0.7 Gm. per kilogram with an otherwise adequate caloric intake was hardly enough to keep a positive nitrogen balance for a four-day period. Studies at this clinic suggest that quantitative as well as qualitative differences may arise when viewing the oral versus the intravenous routes for protein uptake by the body. The quantitative boundaries are rather sharply limned since it requires about fifteen to twenty hours of each twenty-four to drip in the 6,000 c.c. of 5 per cent* amigen solution necessary to provide the nitrogen content equivalent to 225† Gm. of protein. When injected at rates faster or with an increased concentration there is a greater tendency toward unpleasant systemic manifestations. Additional limitations exist. The bulk of fluid necessary as a vehicle for such a quantity of amigen

*This solution is usually made up with a 5 to 10 per cent concentration of glucose.
†Dietary intakes far in excess of this are readily assimilable.

looms large to anyone, but to the patient with a low cardiac reserve it may be insurmountable when reinforced by a sodium content in the amigen solution of such an order of magnitude as to constitute a real problem per se. For the seriously hypoproteinemic individual such hazards appear to be quite as genuine. Qualitative differences are somewhat less clearly definable, yet do seem to obtain. For instance, in a number of our experiments the total nitrogen content of the twenty-four hour urine collection secured after supplying 2,000 to 6,000 c.c. of 5 per cent* amigen solution intravenously (as a slow drip infusion) has been higher than daily total urinary nitrogen values obtained while feeding equivalent quantities of skim milk powder or bovine plasma protein. No broad indictment against nitrogen replacement by intravenous preparations is implied, for no one can gainsay that it has an important role in such therapy. However, since knowledge of the limitations involved, when parenteral clysis is the sole feeding route, seem to be less generally recognized and heeded, this brief discussion appears germane. It is apparent, therefore, that large quantities of intravenous fluids must be injected to introduce enough amino acids for both maintenance of nitrogen equilibrium and promotion of plasma protein regeneration. Any real protein need or other mechanisms for depletion besides inanition, that is, infectious processes, purulent exudates, or ulceration, would promptly and materially increase the requirements necessary for plasma protein regeneration. Without actually achieving this ideal, however, the benefits which can be developed are real and very worth while. . Amino acids alone or, preferably, supplemented with daily doses of plasma (or blood when indicated) make it possible to relieve the steady drain that starvation states and the so often associated depleting mechanisms place on the body's protein stores. This interruption of the patient's autocannibalistic tendencies and a measure of restitution by provision for a liver with improved function, low lipid content, and high glycogen values, both increases an individual's chance to negotiate the hazards of surgical intervention and hastens his convalescence. Such cases of complete obstruction, requiring the outlined therapy, are fortunately in the minority, for they require an inordinate expenditure of patience and time during the tedium of maintaining a prolonged intravenous feeding schedule. It is to be emphasized that in these instances of complete pyloric occlusion the surgeon must speed the preparation. Even in those patients with a high-grade weight loss, therapy should be compressed into a period of ten to fourteen days, for these individuals are most prone to develop pneumonia as a complication of regurgitation, inlying nasal tubes, hypoproteinemia, or mere partial immobilization for long periods during intravenous therapy. Despite these obvious handicaps imposed upon the individual seeking an adequate surgical preparation through parenteral feedings, it is usually possible to culminate the issue successfully by the proper care—and good fortune.

Cases 6 and 7, the patients cared for in the main according to this method, are reported here.

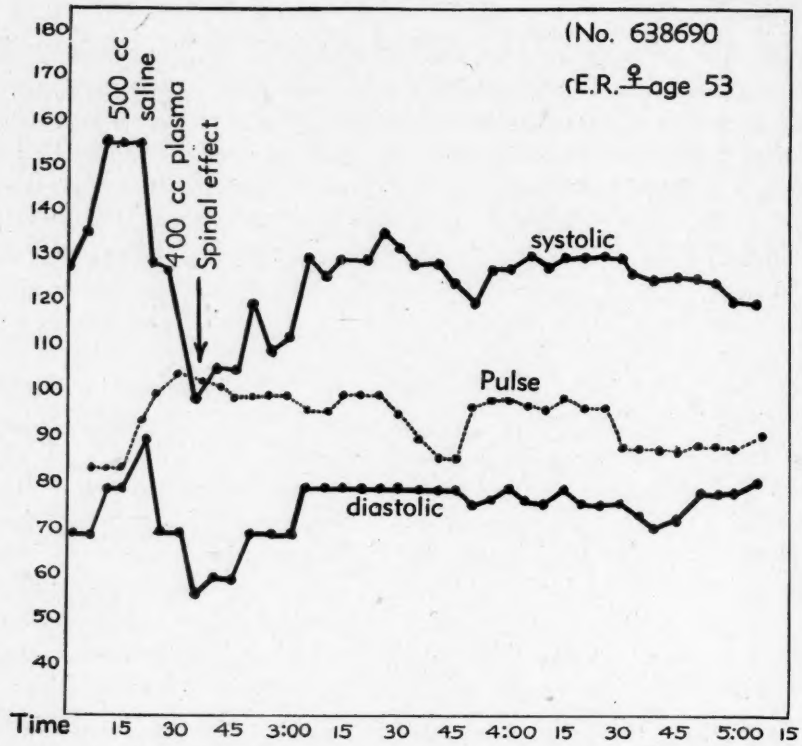
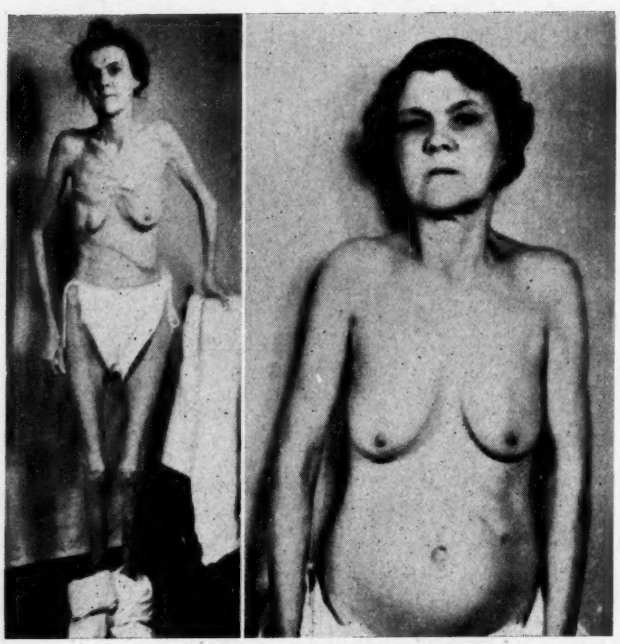


Fig. 9.—Record of blood pressure, pulse, and intravenous fluids during anesthesia. Note stable blood pressure and pulse rate after initial early anesthesia effects (Case 6).



A. *B.*

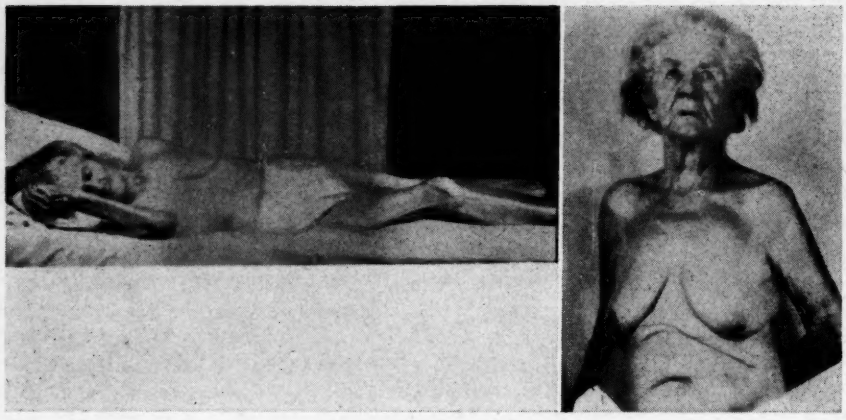
Fig. 10.—Photographs of patient (Case 6); *A*, secured ten days postoperative; *B*, secured three months postoperative.

CASE 6 (No. 638690).—E. R., aged 53 years, for the previous thirteen or fourteen years had had a vague sort of epigastric distress, worse after large meals, relieved by soda, adherence to a bland diet, or vomiting (rarely). Repeated barium meal studies of the stomach and duodenum failed to show any ulcer. During the three weeks prior to admission her vomiting had increased in frequency and followed eating in almost every instance. The weight loss represented 35 per cent of the usual heft and the total body weight was sixty-three pounds. She was unable to walk, talk, sit upright, or feed herself. X-ray pictures secured at this time indicated a very high-grade obstruction at the pyloroduodenal outlet. No commitment as to the exact nature of the lesion could be safely made. During a three-week preparation period the degree of gastric retention varied somewhat from day to day, but in general remained vexatiously high. The dietary preparation, therefore, was achieved, in the main, through intravenous feedings of 20 per cent glucose, amino acids, plasma (or blood), and subcutaneous glucose infusions, daily. About 1,000 c.c. daily of Diet II successfully negotiated the stenotic barrier. The weight gain during this period averaged 1.5 kilograms per week. A subtotal gastric resection was then performed and the obstruction noted to arise from contraction secondary to a benign gastric ulcer. Convalescence was uncomplicated and the patient was discharged on the twelfth postoperative day. This patient gained weight, as can be noted in the follow-up photograph secured several months after the operation, and was in good health until the development of a psychiatric disorder about one year later.

CASE 7 (No. 725261).—A. B., aged 78 years, in the six months prior to admission had had anorexia, vomiting, and about a sixty-pound weight loss, representing 37 per cent of the body weight. When seen at the time of admission she could neither sit, stand, talk, nor feed herself. Every breath was an effort and death appeared imminent. Obstruction was present at the pyloric outlet, but it was possible by combining virtually continuous intragastric drip feedings of Diet II, with 20 per cent glucose, amino acids, and plasma intravenously to achieve a daily intake in excess of 4,000 calories. This schedule was maintained for three weeks with little gain in weight. At that time an 80 per cent resection of the stomach for carcinoma was performed. This procedure was readily tolerated by the patient and she was discharged on the sixteenth postoperative day.

Those Cases With Bleeding.—

Cases Without Obstruction: Patients with bleeding but without obstruction are fed continuously twenty-four hours a day with an intragastric drip of Diet II. Objections have been raised of almost a hypothetical nature, inferring that the presence of a soft rubber catheter may provoke additional hemorrhage by prodding the clot from an eroded but temporarily sealed blood vessel. This conjectured aversion seems more chimerical than real. The presence of a nasal tube provides a feeding schedule every minute, every hour, twenty-four hours a day. This appears to be of extreme importance, for two reasons. First, by bathing the gastric mucosa with a protein mixture the resultant pH of the gastric contents is buffered to values where the acid and peptic effects are appreciably reduced. The following representative figures have been secured. In vitro 100 c.c. of 0.1 NHCL is buffered to pH 3 by 160 c.c. of Diet II and to pH 4 by 225 c.c. In another group of tests after a fasting gastric specimen was secured, dogs were given 0.5 mg. of histamine diphosphate subcutaneously. Samples were then withdrawn every thirty minutes, measured for volume, tested for free acid by titration with 0.1 normal sodium hydroxide using Töpfer's reagent as the end-point indicator and for



A. *B.*

Fig. 11.—Photographs of patient (Case 7), *A*, Secured ten days postoperative; *B*, secured three months postoperative.

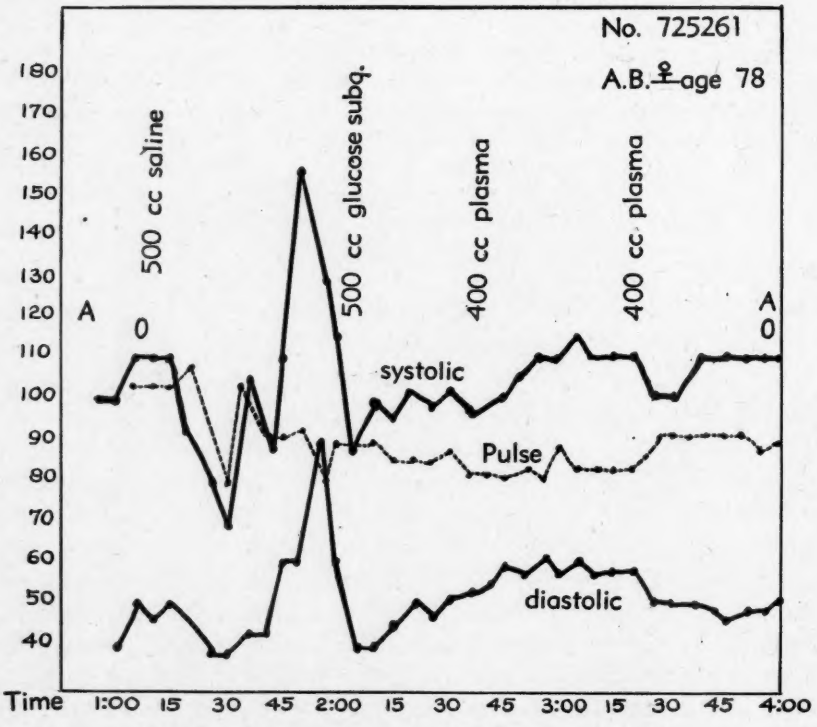


Fig. 12.—Record of blood pressure, pulse, and intravenous fluids during anesthesia. Note stable blood pressure and pulse rate after initial early anesthesia effects (Case 7).

total acid with phenolphthalein as the indicator. Hydrogen ion concentration values were secured with a glass electrode in a Coleman electrometer. When the magnitude of this standard stimulus had been recorded in several animals, the procedure was repeated and 400 c.c. of Diet II were instilled, after securing the fasting sample, and at the moment 0.5 mg. of histamine diphosphate was injected. Each time subsequent samples were removed, several aspirations and flushings were performed as a precaution taken to insure that each aliquot removed was representative.

Two typical experiments are charted here.

Dog 164. Standardizing Test

SAMPLE	DEGREES FREE ACID	DEGREES TOTAL ACID	VOLUME C.C.	PH
1	0	16	4.7	6.01
2	110	118	35.0	1.26
3	127	136	24.5	1.20
4	14	28	1.5	3.51
	After Instillation 400 c.c. Diet II			
1	0	12	1.8	5.92
2	0	118	15.0	4.24
3	0	117	51.0	4.39
4	0	90	32.0	3.57
5	0	114	24.0	4.45

Dog 165. Standardizing Test

SAMPLE	DEGREES FREE ACID	DEGREES TOTAL ACID	VOLUME C.C.	PH
1	0	20	4.6	7.51
2	79	94	48.0	1.46
3	106	118	9.0	1.30
4	72	83	21.0	1.48
	After Instillation 400 c.c. Diet II			
1	0	7	3.3	6.54
2	0	148	32.5	5.24
3	0	137	34.0	4.53
4	0	116	30.0	4.07
5	0	129	28.0	4.95

In this pH range nearly all the acid and 80 to 90 per cent of the peptic proteolytic activity have been controlled. Under such circumstances an initiation of the healing processes is conceivable. Clinical experience has shown that in the absence of obstruction and in the age group under 45 years a gratifying number of operations for bleeding ulcer can be deferred (days if necessary) until the judgment of the surgeon defines the moment for surgery rather than a compelling mandate from uncontrolled bleeding. The second reason for a continuous feeding schedule, and probably of coequal importance with the first, is related to the dividends derived from a very adequate dietary intake. Persons prepared with several days' feeding on a high protein, carbohydrate, caloric, low fat diet, who then must be subjected to an "emergency" procedure, exhibit a greater capacity to withstand both the effects of the bleeding and the operation than do those individuals who, weakened by the bleeding ulcer, are starved as a part of its therapy. Andresen[206] in 1927 was first to propose an active feeding program in bleeding ulcer cases, and he used

rather effectively a gelatin, glucose, cream, milk mixture. The choice of gelatin was unfortunate since it is an incomplete protein, lacking among other amino acids the essential one, tryptophane. To Meulengracht[207-211] belongs credit for arousing a real interest in the issue. At the sixteenth Scandinavian Congress for Internal Medicine in 1933 he reported the first series of cases with hematemesis handled by giving the patient "something to eat." In 1930 and 1935 progressively larger series were reported. In 251 bleeding ulcers there were three deaths (1.2 per cent mortality). His diet consisted of purées, soft foods, and a liberal administration of alkalies. This unorthodox approach to the bleeding ulcer problem intrigued gastroenterologists and was tried at various clinics in America. No group quite attained the remarkable record of Meulengracht but many physicians were able to reduce their local mortality of previous years. The method has not met with universal adoption and debates may linger about certain details, but it is unreasonable to doubt the validity of the major point. It is more scholarly thinking to realize the need for providing a means of neutralizing acid and pepsin, major factors in the genesis and perpetuation of ulcer, than to ignore these items, make no provision for a buffering mechanism, and thereby let nature assume the entire burden of healing, as is done by those who subscribe to the therapy of a starvation regimen. The concomitant advantages secured by providing some nutritious elements are also apparent.

Cases With Obstruction: The problem presented by a bleeding ulcer with obstruction, at times, in any one individual case, may seem almost insoluble. It is common experience that in people with such ulcers almost all methods of neutralization are much less effective. Experience in this clinic with the continuous drip has verified this. Because of the obstruction, feeding by this route may avail little or even be impossible, and bleeding in such circumstances has been very difficult to control. A few times, we have employed a saline solution of human thrombin, instilled into the stomach, allowed to remain in place for twenty minutes, and then repeated every six hours. In this very small series, coincidentally, and for the first time, there has been a prolonged abatement in the bleeding, as indicated by serial hemoglobin, hematocrit studies. Conclusions are unwarranted from such circumstances, which may be merely fortuitous, yet the idea seems to merit repetition. All patients with a bleeding ulcer are transfused several times each twenty-four hours until the hemoglobin is brought up to 10 Gm. and then held at or over this figure. Alkalinization of the urine by an intravenous 5 per cent sodium bicarbonate solution *pro re nata,* in order to prevent tubular precipitation of hemoglobin in an acid media, is a part of this transfusion routine. There has been no cause for regretting adoption of this precaution. Charts of the blood pressure and pulse, secured every hour, are kept on all patients with evidence of any real bleeding. Determinations of the hemoglobin and/or hematocrit are secured at least twice daily and more frequently if at all indicated. And, in spite of these precautions and a real interest in the problem on the part of the nursing personnel, medical and surgical staffs, fatal exsanguination has taken place, without detectable, even

in retrospect, premonitory signs, and hence before remedial therapy could avail. The patient past 45 years of age presents a particularly trying problem. In such instances when recent gross weight loss does not complicate the problem, it is probably wisest to control the bleeding through operative measures as soon as transfusions stabilize the pulse rate and blood pressure outside the shock range. Too frequently in this group a stiffened, arteriosclerotic vessel lies patulous in the ulcer bed permitting life to be pumped away with each heartbeat. When there exists, in addition, a real and obvious need for preoperative nutritional measures due to a recent large percentage weight loss, the problem becomes yet more difficult and any "routine" form of management is disadvantageous. One can stoutly affirm that the decision whether and when to operate on certain patients in this category comes closer at times to divine reckoning than to surgical judgment.

Cases 8 and 9, in which the therapeutics were tailored in quite different fashions, are submitted in partial representation of the dissimilarities existing in the bleeding ulcer problem under altered circumstances.

CASE 8 (No. 677891).—T. O., aged 38 years, had had a duodenal ulcer visualized in roentgenograms obtained at the initial visit five years ago before admission. On that occasion he was bothered by recurrent episodes of epigastric distress, and hematemesis had recently been noted. Despite irregular adherence to a reasonable dietary program for the management of ulcer, his gastrointestinal troubles had been minor until recently. Within the few days prior to admission he had had several large tarry stools and repeated emeses said to include 500 c.c. or more of clotted blood. He was bothered by epigastric pain, persistent, moderate, and unrelieved by food. On admission he was noticeably anemic; tarry fecal residue was present in the rectum. The blood pressure was 120/65 mm. Hg and the pulse was 140 per minute. The hemoglobin was 6.9 Gm. per cent and the hematocrit 17 per cent. He was given 500 c.c. of whole blood at once and the following amounts each succeeding twenty-four hours (the hemoglobin changes have been noted in parentheses for each day's transfusions): 900 c.c. (6.95 to 7.3 Gm. per cent); 1,000 c.c. (8.6 to 8.95 Gm. per cent); 1,500 c.c. (9.3 to 12.0 Gm. per cent). In addition, a continuous drip feeding of Diet II via a nasal tube was instituted. After three days this was changed to a drip feeding of an amino acid mixture for two days and finally a sipper arrangement with Diet II when physical and x-ray findings indicated the patient had developed a right, and possibly left, lower lobe pneumonia. This was cared for promptly by penicillin therapy, and fortunately the bleeding had come under control and could be kept in abeyance with frequent feedings via the sipper arrangement. A subtotal gastric resection was performed two weeks after admission, and eight days later the patient was able to leave the hospital.

CASE 9 (No. 749789).—I. S., aged 61 years, gave a four-year history of recurrent attacks of epigastric distress which appeared to be due to a duodenal ulcer repeatedly demonstrated on roentgenograms and confirmed by an exploratory operation performed elsewhere. Six hours prior to admission, while in another hospital, he had vomited an estimated two quarts of blood clots and blood stained material. Shortly thereafter his blood pressure fell to 70 mm. Hg systolic and he appeared to be in a state of shock. Transfusions of blood and plasma were provided until the pressure rose over 100 mm. Hg, at which time the patient was transported to this hospital. Upon admission the hemoglobin was 12.8 Gm. per cent, red blood cell count 4.09 million per c. mm., and the hematocrit 40 per cent. Eight hundred cubic centimeters of plasma were infused during the course of an emergency gastric resection and the pressure and pulse were stabilized well out of shock range. The convalescence was, unfortunately, complicated by a slight amount of bronchopneumonia.

This condition responded rapidly to penicillin therapy and the patient was able to leave the hospital on the tenth postoperative day.

Cases With Neoplasms of the Colon, Sigmoid, and Rectum

Patients with neoplasms of the colon, sigmoid, and rectum frequently, too, have lost much weight, are hypoproteinemic, present difficult nutritional problems, and indeed the surgical procedure necessary for cure may be of a large order of magnitude. Unfortunately, if the condition has already progressed to the stage of complete large bowel obstruction, no election for the time of surgery is permissible. A proximal colostomy for relief of the distended bowel and deviation of the fecal stream must be performed as soon as possible. In a large group of cases without complete obstruction, whatever interval necessary can be spent in securing an adequate preparation. Application of this principle has helped to enlarge the scope of one-stage procedures in colon

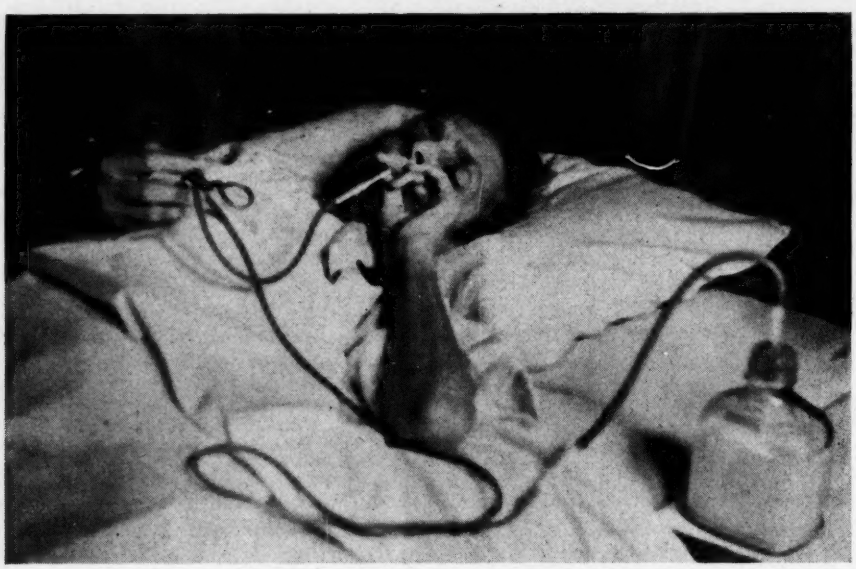


Fig. 13.—Sipper apparatus.

surgery. Diets I and II have been found applicable for the preparation of such patients with neoplasms of the large bowel. Entirely without foresight or deliberate selection, these diets turned out to possess a low fecal residue. In retrospect this could perhaps have been anticipated since the protein and carbohydrate are in highly absorbable forms and virtually no cellulose is present to contribute to the stool bulk. It is not to be inferred that they are non-residue diets; however, the fecal mass, even after the ingestion of large quantities of Diets I and II, is moderate and invariably can be satisfactorily evacuated with cleansing enemas in the final preoperative preparation of the bowel. The effectiveness of this simple method has made catharsis generally unnecessary.

An intake of 5,000 to 6,000 calories daily is urged, with the patient taking whatever reasonable proportions of the Diets I and II offer the greatest per-

sonal appeal. To facilitate feedings among the more enfeebled patients, a simple bedside arrangement has been developed (see Figs. 13 and 14). A two-hole rubber stopper is fitted with a glass adapter for an air vent and an angled glass sipping straw, introduced well through the other opening. To this is connected a section of intravenous tubing, a spring clamp to prevent leakage, and a glass mouthpiece.

The arrangements are completed by filling a flat-bottomed 500 c.c. flask with the desired diet, inserting the rubber stopper, connecting the tubing, and immersing the bottle in a bowl containing ice chunks. The mouthpiece can be loosely fastened within easy reach on the patient's nightgown, while the length of tubing permits the reservoir to rest on the adjacent bed table. The accessibility of this convenience has evoked spontaneous favorable comment

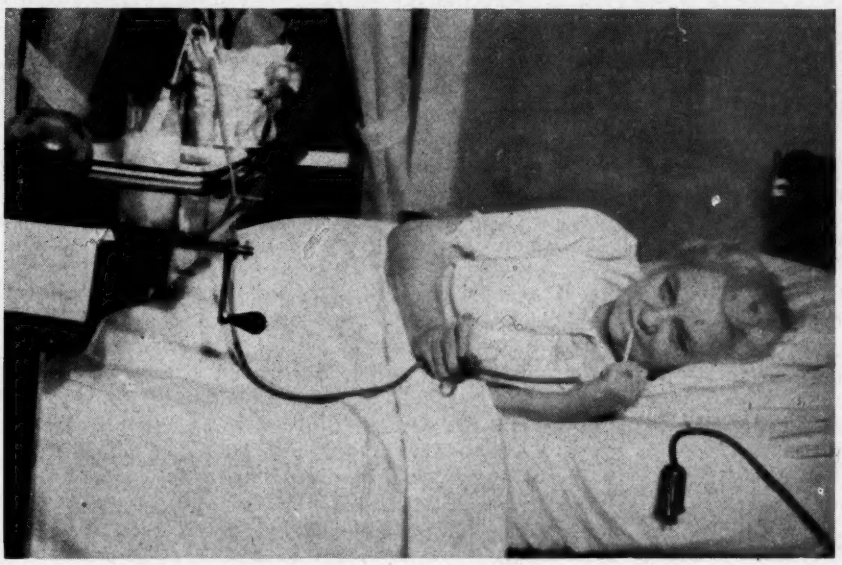


Fig. 14.—Sipper apparatus.

from patients. The gadget promotes an increased awareness that food is at all times easily available, whereas, otherwise, the simple effort of turning over to reach for food on the bedstand may require too much strength and be abandoned unless a nurse or ward maid is available to carry through the desire. At the same time it avoids some of the disadvantages associated with the prolonged use of an indwelling nasal tube.

Cases of Biliary Tract Disease

Patients with lesions of the biliary system where hepatic disease is suspected or proved are prepared by feeding a high protein, carbohydrate, caloric, low fat diet. Most instances of common duct stricture or stone, and invariably whenever carcinoma of the duct or head of the pancreas is the preoperative diagnosis, are so treated. There has been no single instance of postoperative

hepatic failure and the convalescence has seemed uniformly associated with less systemic reaction since the institution of this practice. The diet is not always perfectly tolerated by patients with extreme degrees of biliary obstruction. Adding bile salts to the regimen has helped some, but occasionally the diets cause intolerable distress. We have then supplied as much carbohydrate and protein, by the generous use of plasma and amino acids, as possible by the subcutaneous and intravenous routes.

Three case reports pertinent to preparation in such conditions are presented here (Cases 10 to 12).

CASE 10 (No. 739230).—A. B., aged 36 years, had had a cholecystectomy performed elsewhere six months prior to admission. This was followed by a persistent, rather complete, external, biliary fistula, a subphrenic infection, empyema, and a weight loss slightly in excess of 20 per cent of her usual body weight. The subphrenic infection had largely disappeared at the time of admission. The chronic empyema and external biliary fistula were still present. She was prepared for the biliary surgery by supplementing the regular hospital fare with a sufficient quantity of Diet II to bring her daily caloric intake to more than 4,500 calories. This diet averaged about 250 Gm. of protein per day. In addition, bile salts, vitamins K, C, and B_1, and B complex were provided daily. She gained twenty-five pounds during the several weeks in which this preparation was given and the empyema cured; this cure was effected by establishing complete dependent drainage of the abscess cavity. Postoperatively, after repair of the common duct stricture, some external biliary drainage occurred for a few weeks, but at the time of dismissal this had disappeared, and a cholangiogram indicated that a normal route for bile transit was available.

CASE 11 (No. 726757).—E. J., aged 55 years, had been ill for several years with recurrent bouts of fever and chills. The condition had been treated empirically with sulfonamide compounds, without a diagnosis. During the month prior to admission he had developed anorexia, painless jaundice, a generalized pruritis, and a progressive weight loss. The total weight loss was about 20 per cent of the normal body weight. Nearly every day before admission and during the preoperative hospital stay, he had some fever; this rose on occasion to as high as 104° F. by mouth. On the medical service he received a high protein, high carbohydrate diet of about 2,500 calories daily for about three weeks. He was transferred to the surgical service with the diagnosis favoring a common duct stone. Ten days were devoted to the dietary preparation. Diets IIA and II were used daily to supplement his previous diet so that in excess of 5,000 calories were taken daily. Ample amounts of vitamins B, C, and K and bile salts were added to the oral intake. A Halsted type operation was found necessary when the patient was discovered to have a carcinoma of the ampulla and common bile duct. This included resection of the ampulla, distal portion of the common bile duct, and main pancreatic duct, part of the duodenum, and anastomosis of these ducts back into the duodenal wall. The recovery was without complication. The patient was discharged on the sixteenth postoperative day and has remained well during the ensuing fifteen months.

CASE 12 (No. 733594).—A. W., aged 70 years, five weeks prior to admission developed a painless jaundice, associated with darker than normal urine, light colored stools, a generalized pruritus, and a twenty-pound (about 15 per cent body) weight loss. The clinical diagnosis was carcinoma of the head of the pancreas. The patient was prepared during a period of eleven days for the anticipated biliary surgery by a high protein, carbohydrate, low fat solid diet, plus a liter of Diet II daily. The patient received one transfusion. Vitamins B, C, and K and bile salts were given daily. A single-stage removal of the head of the pancreas, stomach, and duodenum was performed in seven hours and thirty minutes. Throughout the entire procedure the blood pressure was easily maintained at 120 mm. Hg systolic and 60 mm. Hg diastolic, and the pulse rate at 60 per minute, with plasma infused

at a rate equal to the measured blood loss. The postoperative convalescence was hampered and prolonged through an inexcusable technical blunder by myself that resulted in a temporary partial obstruction at the gastrojejunal outlet. At the time of discharge five weeks postoperatively this had cleared up and he was eating a full diet. There was no obvious additional trouble for about six months, but the patient then became cachectic and died.

Cases of Hyperthyroidism

Since the maintenance of normal nutrition in hyperthyroid individuals is hampered by at least two mechanisms (increased rate of utilization and depression of hepatic function) the feeding problem in these cases is doubly important. Weight loss initiated in the past and continuing into the present often, despite therapy with Lugol's solution or thiouracil, bed rest, sedatives, and diets formerly deemed ample, can only be inferred to mean that every day more calories are needed than the individual is ingesting. On the contrary, an uncomplicated gain in weight is a translatable indication that the caloric deficiency has been met. With a growing experience this has come to an ever-increasing significance for us, as a positive sign that such patients, even with severe hyperthyroidism, are ready for any surgery necessary to cure the disease. Stage procedures and polar ligations have found little application in this clinic for more than two years. When the preoperative care has specifically included the use of the high protein, carbohydrate, caloric, low fat Diets I and II, no instance of postoperative thyroid storm has been encountered. Prior to the development of this awareness of the tremendous amount of food that may be required, this complication was encountered. There have been other improvements in the surgical care of hyperthyroid states and therefore it is unfair to suggest that this improvement is related exclusively to modifications in feeding techniques. It does seem pertinent to recount the story of a serious postoperative thyroid crisis, associated with jaundice, hyperthermia, and developing cardiac irregularities, which developed in a patient operated upon without special dietary preparation. During the stormy convalescence, while in an unresponsive condition and with manifest evidence of decreasing hepatic function, he received, among other therapeutic measures, large quantities of Diets II and IIA by nasal tube. Shortly after the institution of this therapy he began to exhibit a gradual progressive recovery with a lowering of the serum bilirubin and general systemic improvement. The dietary feedings were maintained during the remainder of the convalescence which was slow but eventually completely satisfactory. This diet has been tried in another hospital in the management of a severe postoperative thyroid crisis with a similar favorable result.

No further occasions to test the value of this kind of therapy have arisen. Of a certainty, all cases of thyroid crisis do not terminate fatally when no special feeding measures are instituted; yet since the prognosis in this complication is grave, any means possible of benefiting the patient and improving the outcome is worthy of recognition. These patients with severe hyperthyroidism, particularly the exophthalmic variety, are urged to consume sufficient quantities of the Diets I and II, in addition to the regular fare if they so

desire, that weight loss ceases, and better yet, a weight gain is accomplished. This may require 6,000 to 8,000 or more calories every day.

The instance of postoperative thyroid crisis is reported in more detail in Case 13. Other instances of preparation in patients suffering from thyrotoxicosis follow.

CASE 13 (No. 725695).—A. N., aged 55 years, in the year previous to admission noticed a progressive weakness, dyspnea on exertion, excellent appetite but, despite this, a weight loss of fifteen pounds. There was heat intolerance, increased sweating, a tremor of the hands, and prominence in the eyes. A course of deep x-ray therapy to the gland and lugolization had been employed in an attempt to control the hyperthyroidism. Basal metabolic rate determinations during this period were plus 69 per cent, plus 65 per cent, plus 60 per cent, and plus 65 per cent. The ordinary hospital high caloric diet was used in the dietary preparation of this patient on the medical service. His caloric recorded intake, however, was frequently less than 3,500, occasionally less than 3,000 calories daily. Viewed in retrospect, perhaps too little attention was accorded this detail by the surgical consultant and operator. A unilateral subtotal thyroidectomy was performed after fifteen days preparation with Lugol's solution, sedation, bed rest, and this dietary intake. Postoperatively a severe hyperthyroid reaction rapidly developed. The temperature rose to 105° F., jaundice appeared, and the patient was cyanotic and irrational. Thirty-six hours postoperatively, drip feeding with Diet II was started and, augmented by a nearly continuous venoclysis of 20 per cent glucose, more than 6,000 calories daily were provided. Following this therapy there was a steady decline in the serum bilirubin and a gradual improvement in the patient's general condition along with an abatement of the fever. A successful if not smooth convalescence was ultimately secured. Prior to subtotal resection of the gland on the remaining side at a later date, more attention was given to dietary preparation and the recovery postoperatively was without a complication.

CASE 14 (No. 740966).—M. M., aged 35 years, had had a steady increase in the severity of her symptoms of weakness, irritability, nervousness, heat intolerance, sweating, and appetite during the year prior to admission. Many of the classical physical findings of severe hyperthyroidism due to a diffuse hyperplastic goiter were present. The recent weight loss was twenty-five pounds, representing 18 per cent of the body weight. Repeat basal metabolic rate recordings were plus 59 per cent, plus 73 per cent, and plus 53 per cent. Lugol's solution, sedation, bed rest, and a high vitamin B_1 intake were combined with generous portions of Diets I and II, and hospital fare. This patient averaged close to 8,000 calories daily for nineteen days, without significant (less than 0.5 kilogram) weight gain. Bilateral subtotal thyroidectomy carried out after this preparation was followed by an easy convalescence.

CASE 15 (No. 740635).—M. N., aged 64 years, had been bothered by dyspnea and weakness for three to four years before admission. During this interval her appetite had been unusually good. For the past six months she had had insomnia. A known goiter had been present for many years, but lately there was an increase in size of this gland. During the two months prior to admission she noted nausea, would vomit after meals, and found her weakness increasing. Little depression of appetite occurred, however, until this period. A basal metabolic rate secured at that time was plus 50 per cent and a gastrointestinal series of roentgenograms indicated an infiltrating and polypoid carcinoma of the stomach. While awaiting routine admission she developed a lobar pneumonia. Under chemotherapy with sulfamerazine this responded satisfactorily. On the twenty-second hospital day she was transferred to the surgical service. Total weight loss from these several illnesses was over fifty pounds and represented nearly 40 per cent of the usual body weight. It was difficult to make an unequivocal diagnosis of hyperthyroidism clinically. From the laboratory viewpoint there was sufficient gastric obstruction to exclude a galactose tolerance test and the cholesterol

values were of little significance after so much weight loss. Repeat basal metabolic rate studies were plus 78 per cent and plus 56 per cent. Since hyperthyroidism might exist and because she had a moderately severe degree of tracheal obstruction from the nodular gland, thyroidectomy was elected first. A 4,000 caloric diet intake was achieved by using the sipper and Diet II in conjunction with intravenous 10 per cent glucose, amino acids, and plasma (or blood) daily. After two weeks a radical bilateral subtotal thyroidectomy was performed. Recovery was without untoward event. An additional seventeen days were devoted to dietary preparation employing the sipper and Diet II exclusively to achieve a somewhat higher daily caloric intake. An extensive subtotal gastric resection for carcinoma was then carried out. The convalescence was complicationless and the patient was discharged on the ninth postoperative day. There was little weight gain during this preparatory period, but since discharge and return to the outpatient clinic, she has gained steadily and rapidly.

Cases of Burns

The acute need for protein to avoid and to treat the shock rising from burns has been recognized by many.[212-216] It is less generally appreciated that such individuals very soon are in negative nitrogen balance from many causes. Some nitrogen balance studies made in such cases are obviously quite incomplete since no measured values were secured for the amount of protein lost locally from exudation and sloughing.[217, 218] Also, but much less important, no quantitation was made of the protein present in the stool. The intake is reduced by the reluctance of a sick patient to eat. Dressings or pain also may limit the movements attendant with feeding unless special precautions are set up to avoid this situation. There is also an increased nitrogen loss from fever and from the sequestration of necrotic tissues locally at the burn area, as well as from the weeping of protein-containing fluid from the burn site. Unless prompt, effective measures are instituted, these several sources of protein loss may soon generate a severe hypoproteinemia. Wound healing about the burn site is retarded. Of equivalent importance is the fact that split-thickness skin grafts removed from donor sites fail to heal onto these areas. Finally, the donor sites heal slowly or not at all and show an extreme reluctance to grow another full layer of skin. About two-thirds of the total body sulfur is contained in the skin protein. Adults in nitrogen equilibrium[219] on adequate diets can be induced to store considerable amounts of nitrogen and sulfur by superimposition of the proper protein foods on their basal diets. Loss of this material alone from a broadly burned area places a big burden on the protein-synthesizing mechanisms. Diets rich in the sulfur-containing amino acids (methionine and cystine) are particularly necessary, therefore. Patients coming to our plastic service are often already in the stage where they exhibit the chronic effects of the burning. Such patients have been fed diligently Diets I and II, alone or in addition to the regular hospital fare. The beneficial results have become quite apparent. When skin grafting is attempted before adequate nutrition is effected, the results are poorer and healing of all wounds is less satisfactory than when provision is made for an ample period of feeding with a highly protein, carbohydrate, and caloric type diet. Such a feeding program brings about a temporary delay of the necessary reconstructive procedures, but ultimately shortens the required period of hospitalization for a

higher incidence of primary "take" is noted in the grafts, and the donor sites more rapidly regenerate new epithelial layers.

Miscellaneous Conditions

Diets I and II have been applied to the problem of attaining a positive nitrogen balance in a variety of conditions. Its fluid nature is advantageous in the preoperative feeding of patients with esophageal carcinoma. Weight loss from inanition due to obstruction in the esophagus is often a problem in such patients. If necessary a single dilatation can be carried out, but usually the patients are capable of passing on swallows of these liquid diets. From there on the preparation is the same as in all instances of carcinoma of the stomach. Daily intakes of 5,000 or more calories are not unusual. In two instances of esophageal diverticula with a limited food intake associated because of obstruction from the lesion, a nasal tube was threaded past the lesion and the caloric requirements more than met by dripping Diet II into the stomach. Patients with carcinoma of the lip, mouth, tongue, jaw, and neck who are unable to swallow any food postoperatively are satisfactorily sustained in a similar fashion. There is a group of patients with surgical conditions who exhibit a greater tendency to develop diarrhea when oral feedings are urged too vigorously. Included among these are some instances of gastrojejunocolic fistula and regional enteritis, and most of the patients with ulcerative colitis. By exercising moderation and judgment in the pursuance of oral alimentation along with employing Diet II rather than the others in such patients, plus intravenous feedings of glucose, amino acids, plasma (or blood), it has often been possible, nevertheless, to correct amply enough for surgical purposes this nutritional deficiency. In the majority of instances with such preparation, single-stage procedures have been carried through without added hazard. This encompasses a subtotal resection of the stomach, colon, and small intestine followed by the appropriate anastomosis for the gastrojejunocolic lesion, and multiple intestinal resections (often small and large bowel) for the severer cases of regional enteritis. Even the lifesaving procedure of ileostomy for the acutely ill patient with ulcerative colitis, in our experience, is made safer and evokes fewer systemic reactions after adequate efforts directed at nutritional rehabilitation.

As suggested previously, the protein lost through purulent discharges is usually considerable. Patients with a draining empyema, extensive chronic osteomyelitis, or Meleney type of ulceration, are typical of this situation. Such persons are prone to tolerate poorly any necessary surgery. Since an early effect of hypoproteinemia is a contraction of the blood volume, this would conceivably be reflected in an exaggerated response to even slight amounts of blood loss. Our experience has been, though, that if the operation is deferred during a period of dietary preparation, these individuals do then tolerate a very major type of operation. When convinced, by a brief discussion of the importance of their cooperation and the positive contribution they can make by consuming as much of the diet as possible, the patients usually eat large quantities of protein and carbohydrate daily.

Cases 16 to 20 are introduced as evidence that real plasma protein regeneration can be achieved under adverse biologic circumstances. These admittedly are neither exact nor sufficiently critical experiments, yet I believe the data merit consideration for the present and plead successfully the case for additional more detailed observations in the future.

Information pertinent to the protein intake requirements and some of the results obtained by means of daily feedings of large quantities of protein from two sources to a patient with a Meleney type ulcer of the anterior abdominal wall comprise the subject matter in Case 16.

CASE 16 (No. 740032).—K. P., aged 33 years, had a Meleney ulcer, with the edges subcutaneously dissected, which traversed the abdomen from one iliac crest to the opposite side, engulfed the umbilicus, and extended nearly to the costal margin. The progress of the lesion had been associated with a large weight loss, anorexia, febrile episodes, and general bodily and mental deterioration. She was reluctant even to eat when fed by ward attendants, nor would she cry out for medication when in distress. A continuous twenty-four hour a day intragastric drip feeding program with 100 Gm. of powdered bovine plasma* protein in 500 c.c. of water (Diet IV) and sufficient quantities of Diet II to approximate 4,000 calories daily were given. After one week, these quantities were increased to 200 Gm. of powdered bovine plasma protein and enough diet to provide more than 4,800 calories daily. The hemoglobin value, percentage of plasma proteins, and albumin fracture were secured at the beginning of the feeding, during the course of the project, and at its conclusion. Blood volumes were obtained at the start and finish. These data have been recorded in Fig. 15. The most striking rise in the plasma protein value occurred in the albumin fraction which increased from 2.7 Gm. per cent on June 19, 1944, to 3.7 Gm. per cent on July 12, 1944. While the hematocrit rose from 32.5 per cent on June 19, 1944, to 35.5 per cent on July 19, 1944, the blood volume was enlarged from 3.93 to 5.5 liters during the same interval. It is obvious that plasma protein regeneration was effective by this feeding schedule. The magnitude of the quantities regenerated is hardly appreciated until the factor of increased blood volume is brought into the calculations.† It is then apparent that the total albumin content of the plasma volume was nearly doubled during the test period.

Such data serve to emphasize both the hazard of submitting such a patient with a reduced blood volume to any additional bloodletting and the wisdom of providing for restoration of vascularly retained fluids before surgery is undertaken. Interesting, also, is the seeming failure of the body to act effectively on available protein, that is, there is a progressive rise in the intake-conversion ratio. For instance, increasing the protein content of the diet from the average of 295 to 402 Gm. daily actually contributed but 20 Gm. additional daily to the protein retained by the body since the remaining 85 Gm. were lost through an increased daily excretion of urinary nitrogen. In the presence of a real need for protein fabrication the mechanisms controlling this phase of metabolism find limitation in their own processes of conversion, rather than in the digestive and absorptive abilities of the intestine. This impression is corroborated by very low values obtained in analysis of the stool content for protein nitrogen.

*Use of this material is an adaptation to clinical therapy of the data of Madden and Whipple (see Table I).

†See legend, Fig. 15.

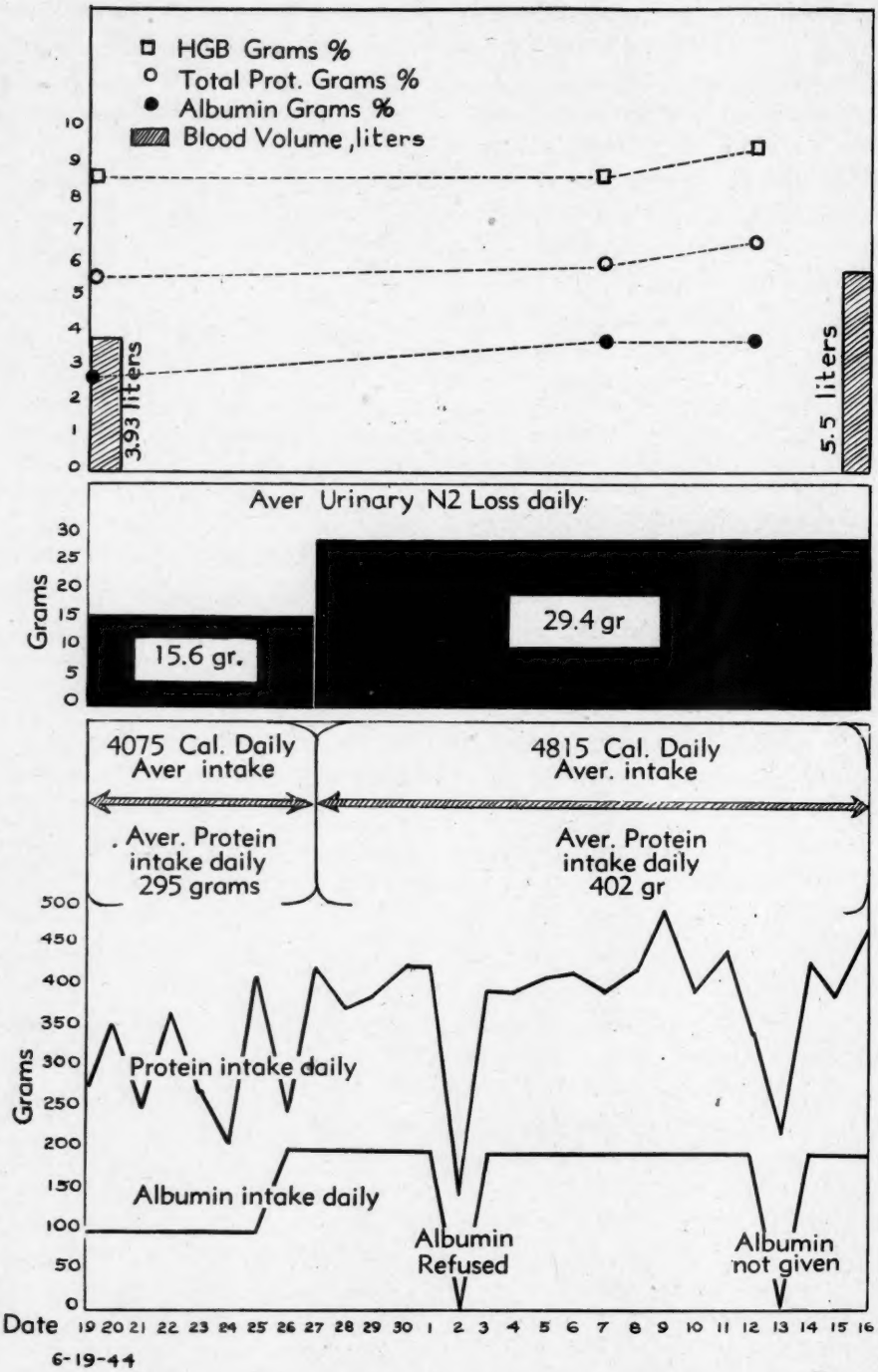


Fig. 15. (Case 16).—Record of total protein intake and plasma protein response. Calculation of albumin gain: blood volume (June 19, 1944), 3.93 liters; hematocrit (June 19, 1944), 32.5 per cent; Plasma albumin fraction (June 19, 1944), 2.7 Gm. per cent; calculated circulating plasma albumin, 71.62 Gm.; blood volume (July 19, 1944), 5.5 liters; hematocrit (July 19, 1944), 35.5 per cent; plasma albumin fraction (July 12, 1944), 3.7 Gm. per cent; calculated circulating plasma albumin, 131.26 Gm.; calculated gain in circulating albumin, 59.64 Gm.

CASE 17 (No. 734359).—F. R., aged 75 years, stated that an indefinite distress in the upper abdomen present for many years had grown during the past two months into an acute, nearly continuous pain, associated with anorexia but no vomiting. Thirty-five per cent of the body weight had been lost recently. X-ray examination of the stomach suggested that a local infiltrating carcinoma of the antrum with retention was present. This degree of obstruction proved to be of no magnitude during the preoperative preparation.

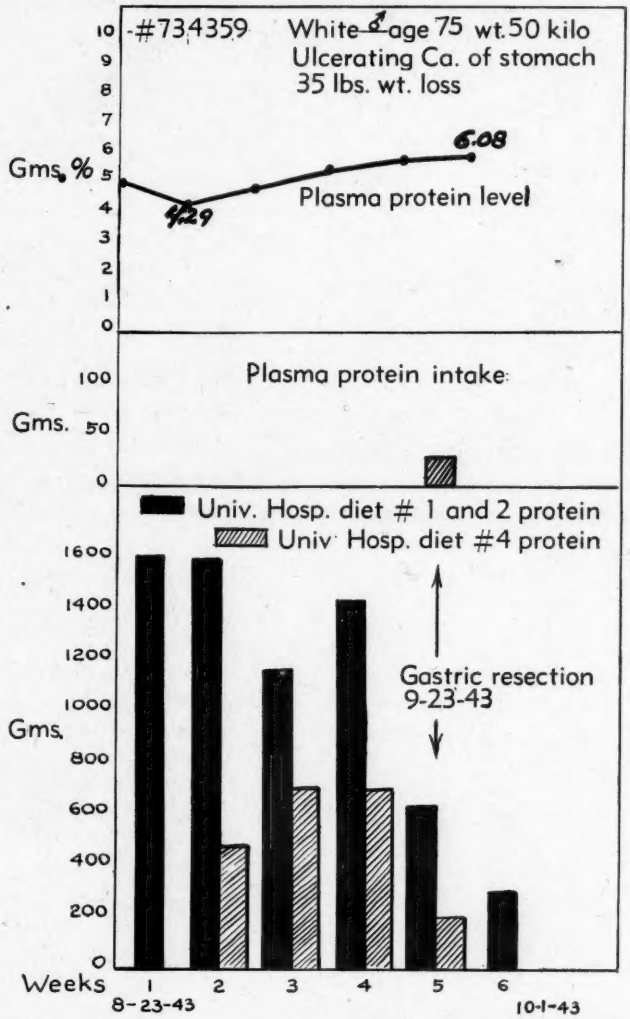


Fig. 16 (Case 17).—Record of total protein intake and plasma protein response.

During the first eight days of dietary therapy nearly 6,000 calories daily were taken in Diets I and II. During this period the plasma proteins dropped from 5.0 Gm. per cent, secured just after beginning the therapy, to 4.3 Gm. per cent one week later. One hundred grams of crystalline bovine albumin in Diet IV were added daily and the caloric intake maintained in excess of 4,000 calories daily with adequate amounts of Diet I. Values for plasma protein secured at approximately weekly intervals during the following twenty-one days were 4.29, 4.9, 5.4, 5.8 (just prior to surgery). (This is about the maximum response

ever secured in these studies from protein feedings with the gastric or duodenal lesion still in situ, to contribute to the regular protein loss.) After this preparation the patient was operated upon, a subtotal gastric resection performed, and a recovery without complications realized. The patient was discharged on the eighth postoperative day.

While studying nutritional problems in surgical patients, the opportunity was realized of treating the hypoproteinemia of a patient with lipoid nephrosis.

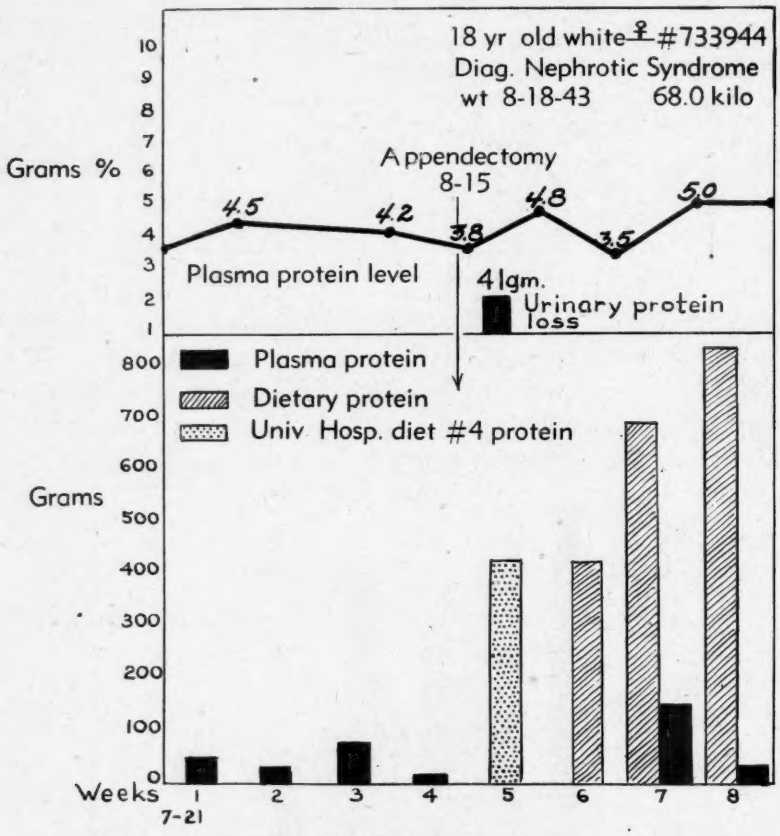


Fig. 17 (Case 18).—Record of total intake and plasma protein response.

Case 18 (No. 733944).—J. S., aged 21 years, was admitted to the medical service, where a diagnosis of lipoid nephrosis was confirmed by clinical and laboratory methods. She developed right lower quadrant pain, tenderness to palpation, and muscle spasm in this region. Appendicitis could not be excluded positively and she was, therefore, operated upon for this condition. During the convalescence she ingested 450 Gm. of powdered bovine plasma protein in Diet IV during a five-day interval, in addition to a diet calorically ample. At the start of the therapy the plasma proteins were 3.8 Gm. per cent. Within twenty-four hours after completing this test period they had risen to 4.8 Gm. per cent. As can be noted in Fig. 17 this gain was achieved despite a urinary loss of about 40 Gm. of protein, determined according to the Esbach technique. At the conclusion of this period she was transferred back to the medical service, where she was placed on salt-free hospital fare with a subsequent steady fall of the plasma proteins to 3.5 Gm. per cent. In excess of 2,250 c.c. of plasma intravenously were then required to restore the plasma

proteins to about the same value they had attained after the feeding of powdered bovine plasma protein.

The apparent increase in the plasma protein value after feeding 450 Gm. of powdered bovine plasma protein might have been achieved through either an increase in the protein intake of the individual or an improvement in the quality of the protein as suggested in the studies of Madden and Whipple. Additional consideration should perhaps have been given to the question of whether the augmented protein intake and subsequent elevation of the plasma proteins were associated with an increased daily loss of protein in the urine. Since the ingestion of the powdered bovine plasma protein was attended by an increase in the plasma protein value, any pyramiding of the urinary loss remained yet small enough to permit a net gain of the plasma protein value. The problem of treating the hypoproteinemia of lipoid nephrosis appears, therefore, intimately related to the quantity of protein ingested and to its innate ability to induce plasma protein regeneration.

Hypoproteinemia, in the absence of ascites, developing in an individual with a Laennec type of cirrhosis, is usually ascribed to an impairment of protein fabrication. While preparing nutritionally just such a patient for the removal of a carcinoma of the colon, observations were made which suggested that under special circumstances even such a pathologically involved liver is capable of elevating a reduced plasma protein value, perhaps even to normalcy.

CASE 19 (No. 723512).—C. G., aged 59 years, was known to have a Laennec type of cirrhosis for at least ten years prior to admission. He had had bouts of jaundice, ascites requiring repeated paracenteses, hypoproteinemia, urobilinuria, and dye retention.

The diagnosis of carcinoma in the sigmoid colon was made before this admission. At that time medical consultants, after securing a number of laboratory tests, noted a depression of hepatic function, probably related to the cirrhosis. For ten days he received on the average of 5,000 calories daily from Diets I and II without raising the percentage of the plasma proteins above the initial level of 5.7 Gm. per cent. During the next nine days the filtered residue obtained from one pound of homogenized raw pork liver was added to the diet, that is, the patient received Diet IIA. This was followed by an increase in the plasma proteins to 6.3 Gm. per cent, an increase associated with augmentation of the albumin fraction as can be noted in Fig. 15. During this second phase of the preparation the caloric intake was maintained high also. After this preparation, exteriorization and excision of the sigmoid lesion was carried out. At the time of exploration the liver was found to be nodular and no larger than the operator's two fists, although the patient's weight was 95 kilograms. Convalescence was smooth from this and from the subsequent closure of the colostomy at a later date. While at home he discontinued the dietary supplement and a fall in the plasma protein value was noted. During this latter hospitalization the patient was again fed the diet containing homogenized raw pork liver, with an apparent elevation of the plasma protein value from 5.25 to 6.3 Gm. per cent. The patient was urged to maintain this special dietary feeding schedule but demurred, finding the diet too unappetizing; about one year after the last surgical procedure he returned on the medical service with an exacerbation of the cirrhosis. Peritoneoscopy at this time indicated a small, coarsely granular, cirrhotic liver.

The data of Madden and Whipple suggest that raw pork liver when fed is capable of evoking a substantial plasma protein regeneration. Under the

special circumstances of a patient with hepatic cirrhosis at least three mechanisms might be involved in accounting for the augmented plasma protein values after feeding the homogenized raw pork liver.

The elevated plasma protein values might be due to: (1) an increased amount of protein in the diet; (2) the introduction of a protein (present in the raw pork liver) which is more efficiently converted to human plasma protein; (3) the ingestion of specific substances in the liver (for example, components of the vitamin B complex) which facilitate plasma protein regeneration either directly or indirectly through improvement of the existing hepatic disease.

The number of patients fed raw pork liver has remained small because the potential danger of causing brucellosis, though remote, is real and therefore can hardly be sanctioned. Pasteurization has not been tried, but would appear to be the best solution to the problem.

CASE 20 (No. 728019).—C. S., aged 53 years, two and one-half months prior to admission, noted a fluctuant area which had developed in the right groin. This had been incised by the local physician but continued to drain and then developed ulceration about the site. The ulcer increased steadily in size, encompassing the entire lower one-half of the abdomen at the time of admission. Bacteriologic studies confirmed the diagnosis of a Meleney type ulceration. She received blood, plasma, and protein in Diet II and protein in the hospital fare. From Fig. 19 it is noted that when this combination of sources was maintained high, there was a simultaneous increase in the plasma protein values. The trauma associated with some necessary surgery for controlling the disease was associated with a fall in plasma protein values. Unfortunately and undoubtedly playing a major contributing role was the contemporaneous reduction in dietary protein since less attention was apparently paid to intake of protein than when the patient was being prepared for the earlier surgery. The values then rose as the diet intake was increased, only to decrease to seriously low levels under a regimen of reduced intake and additional surgery. With the ulcer completely skin grafted by this last procedure, thus removing this source of protein loss, and with an increase again in the total protein intake, there occurred the final elevation of the plasma protein value.

Application of Dietary Preoperative Preparation to Outpatients

Lately the Diet II has been adapted to the nutritional preparation of the patients while at home awaiting hospitalization. Milk powder is secured by prescription from the drug room. The following instructions are then provided. One-half pound of sugar is dissolved in one quart of skim milk, six eggs are beaten into this, and then eight tablespoons of milk powder are completely mixed into the liquid. Vanilla, cocoa, or chocolate syrup, and one teaspoon of salt may be added to bring about a more desirable flavor if wished. The individual is urged to keep this in a clean (preferably boiled) receptacle, under refrigeration. The resulting total amount yielding in excess of 2,000 calories is to be drunk each twenty-four hours, in addition to any other food taken in the diet. It is felt that with such a provision for an adjustment back to an adequate diet, the deterioration of the patient's nutritional status does not continue during the invariable delay between diagnosis and the time a hospital bed is available.

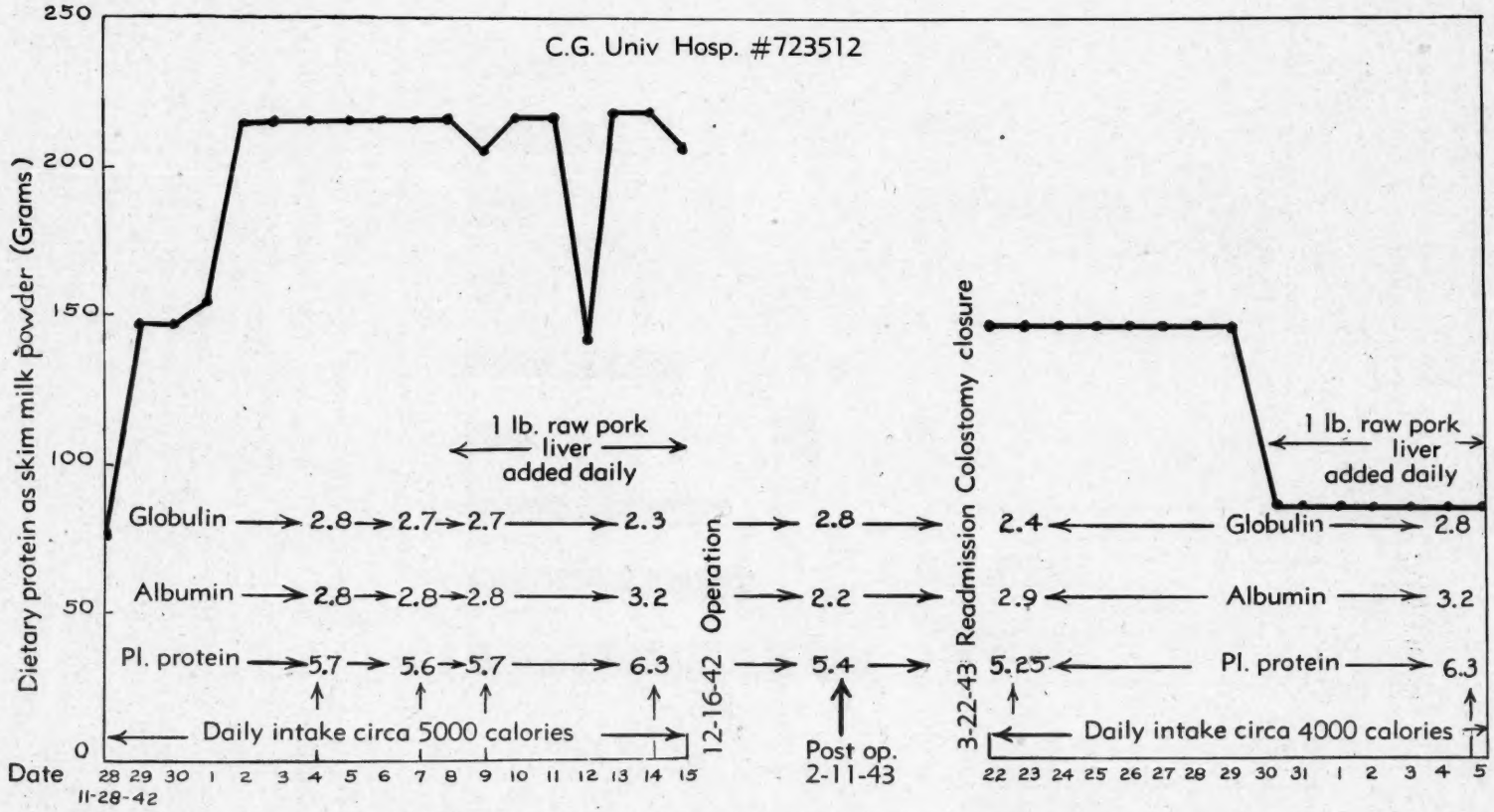

C.G. Univ Hosp. #723512
Dietary protein as skim milk powder (Grams)
250
200
150
100
50
0
1 lb. raw pork liver added daily
Globulin → 2.8 → 2.7 → 2.7 → 2.3
Albumin → 2.8 → 2.8 → 2.8 → 3.2
Pl. protein → 5.7 → 5.6 → 5.7 → 6.3
Daily intake circa 5000 calories
Operation 12-16-42
2.8
2.2
5.4
Post op. 2-11-43
Readmission Colostomy closure 3-22-43
2.4 ← Globulin → 2.8
2.9 ← Albumin → 3.2
5.25 ← Pl. protein → 6.3
1 lb. raw pork liver added daily
Daily intake circa 4000 calories
Date
28 29 30 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
11-28-42
22 23 24 25 26 27 28 29 30 31 1 2 3 4 5

Fig. 18 (Case 19).—Record of total protein intake and plasma protein response.

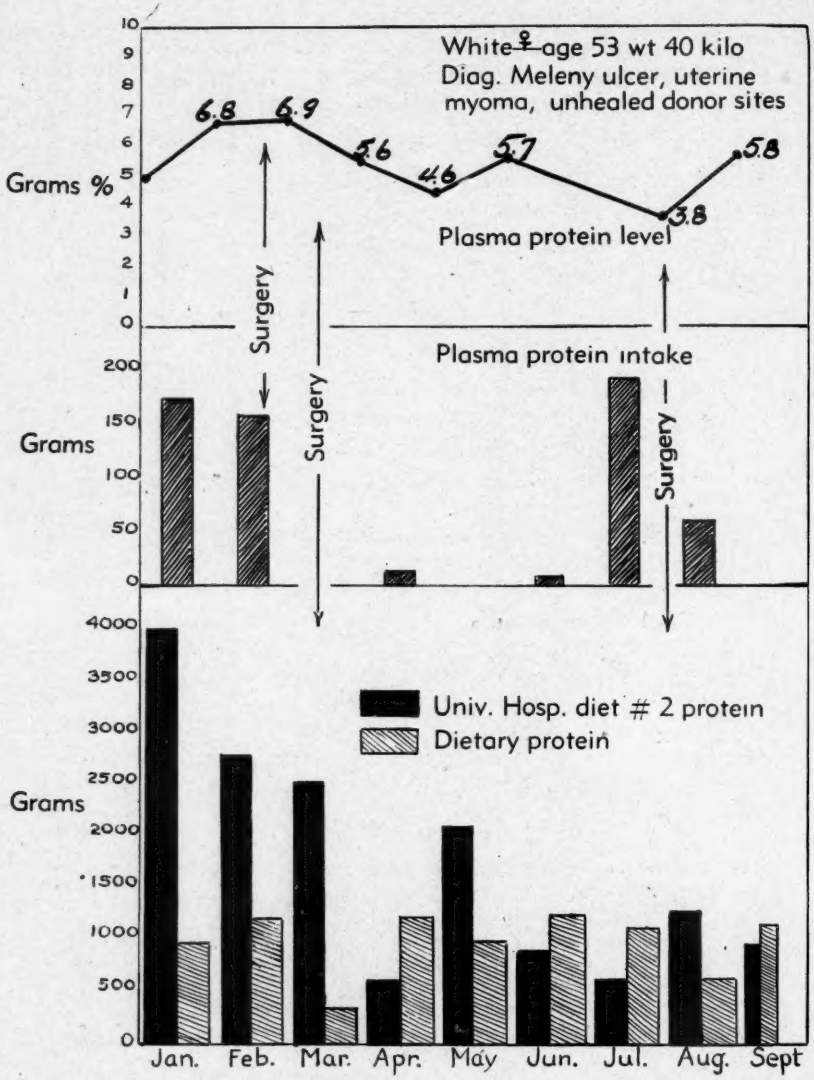


Fig. 19 (Case 20).—Record of total protein intake and plasma protein response.

CRITERIA FOR JUDGING DURATION OF FEEDING PROGRAM

Unfortunately, no method of precision is at present available to guide the surgeon in deciding on the length of time preoperatively each patient should be prepared nutritionally. It can, however, be readily appreciated from the foregoing discussion that the loss of body weight is of paramount importance in this calculation. More specifically, the percentile weight loss is the most important and reliable single determining clue found to date. After a limited trial, it appeared that the correlation between biopsy samples secured with the Silverman needle prior to therapy and again at the time of surgery was not enlightening. More efforts are required though to crystallize

this impression. Larger pieces than can be obtained through this type needle, which would be susceptible of quantitative organic chemical analysis, might possibly yield information more readily interpretable. Without submitting patients to an unnecessary operation, no way, as yet, has been found for securing the required control specimens.

Using the percentage body weight as the best index so far encountered, we have come to rely upon the following temporal estimates.* It is admitted that these are rather empirically selected. However, a growing experience gained from the application of these time intervals to several hundred clinical cases suggests that they are at least long enough to permit an adequate dietary preparation for the most extensive type of surgery.

1. When the percentage of body loss is at least 5 to 10 per cent, three to five days of proper feeding is sufficient.

2. When the percentage body weight loss approaches 20 per cent, ten to twelve days of proper feeding are necessary.

3. When the percentage body weight loss approximates 25 to 30 per cent, nearly three weeks of adequate feeding are required.

4. When the percentage weight loss is in excess of 35 per cent, at least one month of thorough feeding is needed. In this classification is included patients too weak to sit, stand, talk, or feed themselves. When prepared according to this schedule, they are customarily discharged from the hospital after about the same length of postoperative sojourn as those without such a handicap to overcome.

SUMMARY

In summary it may be stated that the application to clinical material of the wealth of carefully acquired and accurately documented biologic information on the pathologic physiology of starvation states has been woefully neglected. The therapeutic problems initiated by starvation states are broad and touch on many aspects of the surgeon's sphere of activity. A failure to recognize and appreciate the importance of the concomitant effects that may develop from an inadequate nutrition (fatty liver, decreased hepatic function, hypoproteinemia) materially pyramids the hazards of surgery in that individual. On the contrary, an adequate preparation with appropriate diets lessens significantly these dangers. Without such preparation, the surgeon either must refuse these individuals even surgical procedures of necessity, because of the appreciated added hazards from such an undertaking, or, when persuaded to operate during a default in judgment, he is often led into tragic consequences. On the contrary, we have come to believe that these "poor-risk" cases can be conscientiously accepted for operative procedures of almost any magnitude tolerable to standard-risk cases without augmenting seriously the risk accepted by them—if good dietary preparation has been achieved. From much animal experimentation, it was inferred that a diet rich in proteins, carbohydrates,

*In individuals with complete pyloric obstruction, being fed exclusively by the parenteral route, it is often wisest to compress the preparation into a fourteen- to sixteen-day period.

and calories, but low in fat would be most likely to afford the greatest protection and provide the best nutrients for restoration to normalcy of the involved structures. Diets have been proposed which embody these considerations. The high protein content has been achieved by fortifying several vehicles with milk powder, which contains all the essential amino acids. Similarly, lactose, cane, beet sugar, are cerelose was added to attain the high carbohydrate content. The fat content has been reduced to minimal values. The two diets developed on this plan most frequently employed are Diets I and II. Diet I is palatable and comes in multiple servings during the day. Diet II is designed to function for tube feedings, is less palatable, but is taken readily by mouth by almost all patients. These diets have been used in the routine care of several hundred patients hospitalized upon both a general and a gastroenterologic surgical service. Large quantities, by volume and caloric content, of such formulas were found to be well tolerated. They have appeared to exert very beneficial effects in correcting some of the pathologic changes secondary to an inadequate, poorly selected caloric intake. Preparation with such diets has been the added factor which permits the surgeon greater license in the magnitude of the operative procedure he may undertake for a cure, and greater freedom to extend the indications for palliative surgery, all without accepting a discouraging increase in mortality. With vigilant attention to such details as hemostasis, blood and plasma replacement commensurate with manifest losses, and careful maintenance of the proper depths of anesthesia, the surgeon can complete his task in a leisurely, meticulous fashion free of the obligation to operate "with an eye on the clock."

These details have also functioned to improve the ravages of bodily structure caused by a wide variety of disease conditions per se (burns, empyemas, Meleney ulcers). Suggestions have been offered to guide the preoperative dietary management of surgical patients with diseases of the gastrointestinal tract.

Particular emphasis was placed on the therapy for lesions of the stomach and duodenum. The special problems related to pyloric obstruction and bleeding associated with lesions in this region received detailed comment and tested therapeutic hints were appended. Feeding of Diets I and II was noted to be a satisfactory form of preparing nutritionally the majority of patients with surgical conditions encountered in the intestinal tract. The bowel residue after such feedings was found to offer no problem during required colonic surgery. This method of preparing patients was applied to those with disease of the biliary tract (stone, stricture, or carcinoma), in instances of hyperthyroidism, and several other surgical conditions. The impression was expressed that recovery from the surgery was more certain and the convalescence more swift than when such dietary preparation was neglected.

The percentage body weight loss is believed to be the best single consideration in determining the duration of the feeding program. Estimates, relative to this percentage weight loss, of the length of time the feeding period should be continued are suggested. Precise functional tests or crucial experimental

proofs of these considerations, however, have not been, as yet, attainable. Man, even under ideal conditions, is a difficult biologic organism to standardize. The problem is additionally complicated by the several hiatuses that exist in our knowledge of protein metabolism generally and specifically in human beings. Since, also, several of those mechanisms originally producing the functional derangements of metabolism (fatty liver, hepatic dysfunction, hypoproteinemia) continue to influence unfavorably normal processes during periods when, through diet, the re-establishment of normal metabolism is sought, the ultimate result will be the balance attained by destructive and constructive forces. Our present efforts suggest, but with no more concrete proof than that of clinical results, that major efforts directed at nutritional readjustment can be made to yield a margin of safety for the patient requiring surgery, in spite of previous, and with coexisting deleterious influences on, metabolic processes. It is apparent that such measurements should be secured; in particular, the rate of development and reversal of pathologic cellular changes in the liver, information concerning the factors governing these changes, knowledge of the intimate regulating mechanisms accelerating and depressing protein anabolism.

Despite the lack of confirmatory evidence obtained under rigid experimental conditions indicating that dietary preparation lessens the risks of formidable operations, the clinical evidence on this score is overwhelming as suggested in a number of the case reports detailed in this study. It has been pointed out that patients who have lost considerable weight are not good candidates for operations of magnitude after adjustment of water, electrolyte, and hemoglobin values. On the contrary, if, in addition, the nutritional deficit of the patient is repaired, such patients tolerate prolonged operation well. Adequate dietary preparation of poor-risk patients who have lost considerable weight does away with the element of hurry in operations. These lessons learned in the school of experience when adopted as standard practice in the preparation of surgical patients will have a telling favorable influence in extending the benisons of surgery to borderline groups of surgical risks without increasing materially the surgical mortality. The surgeon must school himself in the intricacies of dietary preparation of patients as well as in evaluating water and electrolyte balance and in mastering surgical technique.

CONCLUSIONS

1. Many patients with gastrointestinal lesions remediable by some surgical procedure present nutritional problems.

2. When a large amount of body weight has been lost by such an individual, the hazards of surgery are increased.

3. Surgery in these patients can be performed at approximately the same mortality as in the standard-risk patient when adequate dietary preparation has been achieved.

4. An adequate dietary preparation can be achieved in these patients, especially when no obstructive element is present, by the utilization of high protein, carbohydrate, caloric, low fat diets.

5. Diets described in the text fulfill these criteria and perform satisfactorily this preparation.

6. Special dietary problems are posed by the patients with obstruction at the gastroduodenal outlet.

7. A satisfactory nutritional preparation can usually be achieved in these patients by employing methods outlined in this study.

8. Special problems of feeding and hemostasis are involved in those patients with bleeding ulcers of the stomach and duodenum. These problems are related to the severity of the hemorrhage, the age of the patient, and presence or absence of obstruction. Suggestions are offered relative to the care of such patients.

9. The need for, and applicability of, such diets in the nutritional preparation of a variety of surgical states is discussed.

10. Broad, empirical rules (but so far the best indices we have) based on the percentage of total weight lost are proposed.

11. The need for securing incontrovertible proof, under better controlled experimental conditions than the clinic affords of the observations related herein, attesting the value and importance of adequate dietary preparation of surgical patients, is suggested.

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ALKALINE PHOSPHATASE AND METASTATIC LIVER DISEASE

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ALKALINE phosphatase as a diagnostic aid in metastatic carcinoma in the liver has been recorded in the past few years.[1, 2] While serving as a resident on the surgical service of the Presbyterian Hospital of Chicago, I had the opportunity of studying another series of cases, which is the subject of this communication. This test has been employed on all patients with carcinoma on whom it was anticipated there would be an exploratory operation in order that our clinical findings might be checked with the laboratory.

Alkaline phosphatase has been found in greatest amount in osteogenic tissue, renal epithelium, and epithelium of the small intestine,[3] thus, tissues involved in bone formation or in glucose absorption or elimination. It is not found in normal liver cells or bile ducts.

It is possible to produce a carcinoma of the liver in rats by feeding them dimethylaminoazobenzene.[3, 4] In their normal liver endothelium phosphatase is present in small quantity while there was a large amount of the phosphatase found histologically in the endothelium between the newly formed carcinomatous duct tissue. Even the cytoplasm of the carcinoma cells in the liver contained it. This latter may, however, be a specific reaction peculiar to the species since the same tumors reproduced in mice failed to show the high phosphatase content.[5]

In human beings,[3] very little phosphatase was shown in a carcinoma of the breast, whereas it was found in abundance in an adenofibroma and in normal lactating breast tissue. Furthermore, the only phosphatase in a sigmoid carcinoma was found in the surrounding vascular endothelium while in the metastases it was marked in the surrounding endothelial tissue. The hypothesis of these authors concerning the presence of the phosphatase about vascular endothelium was that this tissue contributed to or removed it from the blood stream.

Since it is known there are many forms of liver disease which will give rise to a high alkaline phosphatase, theories have been proposed to account for this. One concept is that the retention of enzymes is due to anything which blocks the excretion of the particular organ. Thus it would be expected that biliary obstruction due to a common duct stone would produce a high phosphatase. This occurs. Other theories maintain that the increase is due to altered liver function. Whether tumor nodules would actually block phosphatase excretion is not known and as yet it cannot be stated just how the phosphatase rises with biliary obstruction.

With this work in mind we have followed eighty-five consecutive cases of carcinoma taking an alkaline serum phosphatase level in each case in an

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TABLE I. CARCINOMA WITH LIVER METASTASES AND HIGH ALKALINE PHOSPHATASE

CASE NO.	AGE (YR.)	SEX	PHOSPHATASE	PER CENT PROTHROMBIN	DISEASE	REMARKS
7	56	M	36.0	--	Carcinoma of rectum	Liver filled
17	49	F	34.5	--	Carcinoma of rectum	Liver filled
26	54	F	30.0	100	Carcinoma of sigmoid	Liver filled
35	47	M	22.8	--	Carcinoma of sigmoid	Many nodules
36	54	F	24.9	--	Carcinoma of rectum	Many nodules
37	56	M	21.8	70	Carcinoma of rectum	Liver enlarged at death
57	48	M	30.0	100	Carcinoma of rectum	Liver filled, found at cholecystectomy, carcinoma 3 yr. before
61	55	M	22.5	80	Carcinoma of rectum	Liver filled
62	49	F	49.8	--	Carcinoma of rectum	Liver filled
72	41	F	30.0	80	Carcinoma of breast	Liver filled at autopsy
76	66	M	48.6	75	Carcinoma of sigmoid	Liver now nodular, icteric index 84
77	49	M	21.3	--	Hypernephroma	Liver filled
84	66	M	14.2	--	Carcinoma of rectum	Liver filled
92	57	M	15.7	--	Carcinoma of liver	Liver filled
93	48	F	34.5	80	Carcinomatosis	Liver filled

TABLE II. CARCINOMA WITH NORMAL LIVER AND HIGH PHOSPHATASE, ELEVATED ICTERIC INDEX

CASE NO.	AGE (YR.)	SEX	PHOSPHATASE	PROTHROMBIN	DISEASE	REMARKS
34	56	F	14.2	--	Carcinoma of rectum	Postoperative peritonitis, icteric index 24 taken at time of phosphatase
46	48	M	42.0	90	Carcinoma of ampulla of Vater	Liver free, icteric index 132
75	67	M	90.0	70	Carcinoma of duodenum	Liver free, icteric index 15

TABLE III. CARCINOMA WITH LIVER METASTASES AND NORMAL PHOSPHATASE

CASE NO.	AGE (YR.)	SEX	PHOSPHATASE	PROTHROMBIN	DISEASE	REMARKS
4	63	F	9.3	100	Carcinoma of rectum and ovary	Many liver nodules
11	57	M	9.3, 6.3	60	Carcinoma of rectum	Several nodules
14	67	F	6.7	100	Carcinoma of cecum	Several nodules
27	63	M	8.2	100	Carcinoma of cecum	Few nodules
32	39	F	4.8	--	Carcinoma of breast	3 large nodules and multiple bone metastases
53	53	M	4.1	100	Carcinoma of cecum	Many nodules

TABLE IV. CARCINOMA WITH A QUESTIONABLE NODULE IN THE LIVER AND NORMAL PHOSPHATASE

CASE NO.	AGE (YR.)	SEX	PHOSPHATASE	PROTHROMBIN	DISEASE	REMARKS
9	52	F	8.2	100	Carcinoma of sigmoid	Single nodule, questionable
22	70	M	2.7	40	Carcinoma of rectum	Single nodule, questionable
50	30	F	3.1	--	Carcinoma of rectum	Single nodule, questionable
82	62	F	7.7	100	Carcinoma of ascending colon	Single nodule, questionable

attempt to predict liver involvement. We have twenty-six cases in which carcinoma was not the problem but where the patient was hospitalized for other disease and used as a control or had known liver disease other than metastases. These 111 cases have all been proved by exploration or, in a few cases, by autopsy.

TABLE V. PHOSPHATASE READINGS IN PATIENTS WITH LIVER DISEASE OTHER THAN CARCINOMA

CASE NO.	AGE (YR.)	SEX	PHOSPHATASE	PROTHROMBIN	DISEASE	REMARKS
1	55	F	70.5	90	Common duct obstruction	Long-standing jaundice icteric index 20
2	56	M	25.8	100	Catarrhal jaundice	Icteric index 171
3	58	M	45.7	100	Hypertrophic cirrhosis	Icteric index 19
8	57	F	22.8	--	Common duct stone	Icteric index 12
16	54	M	26.2	--	Cholecystitis	Icteric index 18

Of the 85 cases, wherever we found the alkaline phosphatase elevated (King Armstrong units, 13 being the upper limit of normal) and ruled out certain other diseases such as cirrhosis, obstructive jaundice, or bone disease, there was metastatic disease in the liver. There were fifteen cases which fell into this category although one of these patients had jaundice with the metastases whereas the others did not.

TABLE VI.* PATIENTS WITH CARCINOMA

Number of patients	57
Liver	Normal
Phosphatase	Normal

*Individual cases not charted.

In our series there were six cases in which there was definite, and at times marked, liver involvement with a normal phosphatase. We are unable to explain these findings. There were additionally four patients with a questionable single, small liver nodule and a normal phosphatase.

TABLE VII. NORMAL PATIENTS

Number of patients	21
Liver	Normal
Phosphatase	Normal

An attempt to correlate prothrombin determination with liver involvement gave no findings of significance.

In conclusion, as a routine test when dealing with a known malignancy and in the absence of jaundice, known liver disease or abnormal osteogenic activity, a high phosphatase will probably help in establishing the operability of a surgical case. Perhaps a more important use will be in checking postoperative patients to determine late liver involvement without subjecting them to exploration.

SUMMARY

1. Alkaline phosphatase in a series of eighty-five cases of carcinoma is presented.

2. Where there was a high phosphatase—and other forms of liver disease such as obstructive jaundice, cirrhosis, and bony involvement could be ruled out—the test showed metastases in all of our cases.

3. Normal phosphatase, however, does not rule out liver metastases.

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PULSATING HEMATOMA, FALSE ANEURYSM, AND ARTERIOVENOUS FISTULA DUE TO WAR INJURIES

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THIS presentation is not meant to be an exhaustive treatise on the subject of vascular injuries and their sequelae in battle casualties. Rather, it is an analysis of experience with vascular injuries on the surgical service of this general hospital in the Southwest Pacific Theater of War to which casualties were admitted from the campaigns for the Philippine Islands. Four thousand and forty surgical battle casualties (wounded in action) were admitted to this general hospital over a five-month period of time from Oct. 25, 1944, until March 25, 1945. Included with these were twenty patients with severe injury to the peripheral vascular channels of the torso or extremities resulting in false aneurysm, pulsating hematoma, or arteriovenous fistula. The incidence of traumatic vascular lesions of the peripheral circulation in this series of cases is .49 per cent. The types of vascular lesion are listed in Table I.

The diagnosis in these cases, the surgical management, the presence of complications such as nerve injury, contracture of joints, or secondary hemorrhage, and the indications for surgical intervention presented a variety of problems, the solutions of which were intensely interesting as well as challenging. Bearing in mind the dictum that, in the management of vascular injuries, operation should be postponed until collateral circulation has been established so that major vessels may be ligated and divided safely, attention was directed primarily toward the healing of wounds and the establishment of collateral circulation. However, it was necessary to operate upon fifteen of these patients at this general hospital. Early operation was performed only in those patients in whom external or internal hemorrhage endangered life or the viability of an extremity, in those in whom contracture developed rapidly, or in those in whom there was progressive paralysis of peripheral nerves intimately in association with the vascular lesions.

In these twenty patients in whom arteriovenous fistula, false aneurysm, or pulsating hematoma developed as a result of war wounds, the majority of the injuries were caused by small caliber bullets or small shell fragments. Eleven of the vascular tears were caused by Japanese artillery shell fragments, five by Japanese .25 caliber rifle bullets, one by a .30 caliber rifle bullet, two by .31 caliber Japanese machine gun bullets, and one by a .50 caliber machine gun bullet.

ARTERIOVENOUS FISTULA

There were ten arteriovenous fistulas. Seven of these were caused by Japanese artillery shell fragments, two by Japanese .25 caliber rifle bullets, one

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TABLE I. TYPES OF VASCULAR LESIONS

LOCATIONS	NUMBER OF CASES
Arteriovenous aneurysm	8
Arteriovenous aneurysm and secondary pulsating hematoma	2
False aneurysm	4
False aneurysm and secondary pulsating hematoma	2
Pulsating hematoma	4
Total	20

by a .30 caliber bullet. Hemorrhage from the wound at the time of injury was severe in three patients, mild in six, and insignificant in one. The diagnosis was established by the detection of a to-and-fro murmur at the site of swelling prior to admission to this hospital in only five of the patients. In three the diagnosis was established for the first time on the day of admission to this hospital and in two the bruit was not heard until two weeks after admission and approximately four weeks after injury. In these cases the area of the swelling was examined with a stethoscope but no bruit could be heard in the early weeks following injury. As the days passed, a to-and-fro murmur became audible and increasingly intense, coincident with the development of venous dilatation. It is thought that these were cases of pulsating hematoma which subsequently developed into arteriovenous fistula. In three cases a metallic foreign body had been removed from the extremity prior to the admission of the patient to this hospital. Débridement had been done in the forward areas on only one of these wounds.

Listed in Table II are the locations of the arteriovenous fistulas or aneurysms between concomitant arteries and veins.

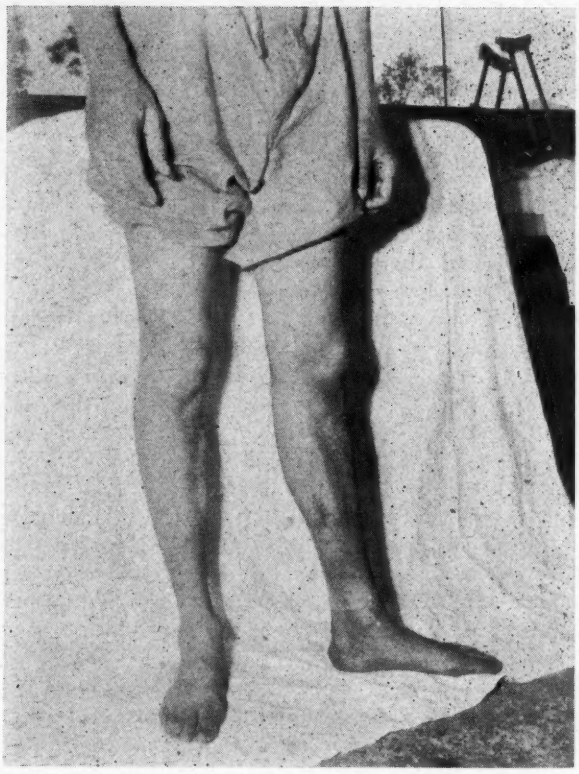
TABLE II. LOCATIONS OF ARTERIOVENOUS FISTULAS OR ANEURYSMS

LOCATIONS	NUMBER OF CASES
External iliac artery and vein	1
Femoral artery and vein, middle third	3
Femoral artery and vein, upper third	1
Posterior tibial artery and vein, middle third	2
Posterior tibial artery and vein, lower third	1
Internal carotid artery and jugular vein	1
Brachial artery and vein, lower third	1
Total	10

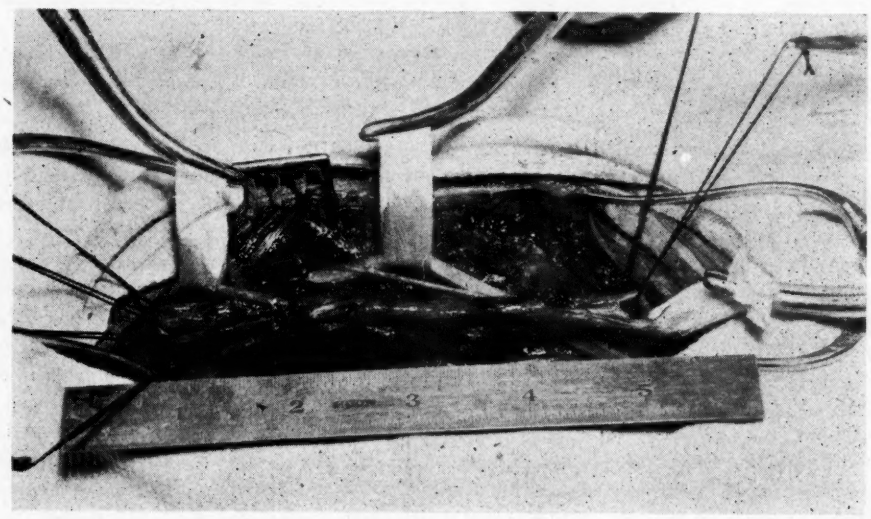
CASE REPORTS

Arteriovenous Aneurysm of the Posterior Tibial Vessels

CASE 1.—A 27-year-old infantryman was struck in the left leg by a .25 caliber Japanese rifle bullet on Oct. 20, 1944. The missile entered the posterolateral aspect of the calf in its middle third and lodged subcutaneously on the medial aspect of the calf at the same level. Surgical débridement was not done but the wound was dressed with sulfanilamide powder. On November 6 the bullet was removed under local anesthesia. Scar of the operative incision is shown in Fig. 1, *A*. Troublesome hemorrhage from the wound was controlled by suture of the incision. Twenty-four hours after this operation, sedation by morphine was necessary because of pain about the operative site. On examination at this hospital on November 27, there was a palpable thrill over the elevated tissue about the scar on the medial aspect of the



A.



B.

Fig. 1 (Case 1).—*A*, Photograph showing the scar of the left leg which represents the site from which a bullet was removed before the diagnosis of arteriovenous fistula was made. The operative note stated that there was "profuse bleeding" at the time of the removal of the foreign body. Although the fistula was a large one which afforded communication between the posterior tibial artery and several concomitant veins, there is no superficial venous dilatation. *B*, Photograph taken at the time of operation shows an arteriovenous aneurysm between the posterior tibial artery and several adjacent veins. The umbilical tape on the right supports the proximal posterior tibial artery. That in the middle retracts the posterior tibial nerve and the tape on the left identifies the posterior tibial artery distal to the aneurysm. The silk ligatures identify three veins proximally and four veins distally, all of which communicated with the aneurysm.

calf. A to-and-fro bruit could be heard over this area. The dorsalis pedis and posterior tibial pulses were palpable. There was no difference in the blood pressure in the two lower extremities. Oxygen saturations of specimens of venous blood from the right and left femoral veins were 60 and 70 volumes per cent, respectively. Teleroentgenograms of the heart taken at a six-foot distance showed no cardiac enlargement and no change in cardiac diameters when the fistula was compressed. The pulse rate dropped from 80 to 74 beats per minute when the fistula was compressed. Blood pressure before manual occlusion of the arteriovenous fistula was 120/64 and after occlusion it was 130/70. There was hyperesthesia over the dorsum of the left foot. Progressive increase in the degree of swelling was noted. In preparation for operation the popliteal artery was compressed against the head of the tibia for fifteen minutes four times a day. On January 9 the lesion was excised at operation. Fig. 1, *B* is a photograph taken at the operating table. The arteriovenous fistula represented a communication between the posterior tibial artery and several adjacent veins. The opening in the artery was at a point just distal to the branching off of the posterior peroneal artery. The fistula had enlarged to an aneurysm measuring one inch in vertical and one-half inch in transverse diameters. Three veins communicated with the aneurysm on its proximal end, and distally there were four communicating veins. The posterior tibial nerve was adherent to the aneurysm but its continuity was intact and there was no neuroma. The aneurysm was excised after secure ligature of the afferent and efferent arteries and veins. It was interesting to note that measurements of the diameters of the artery and the largest vein were as follows: proximal artery ⅛ inch, proximal vein ¼ inch, distal artery 3/64 inch, distal vein ¼ inch. After excision of the lesion the distal stump of the posterior tibial artery pulsated forcibly. The circulation in the foot was so good following operation that block of the lumbar sympathetic ganglia was not deemed necessary. The patient made an uneventful recovery and was transferred to the United States for further convalescence two weeks after operation.

In this case the bruit undoubtedly was present from the time of injury and the operative removal of the bullet probably was the cause of secondary enlargement of the arteriovenous fistula.

Arteriovenous Aneurysm of the Posterior Tibial Vessels With Subsequent Rupture and the Development of Secondary Pulsating Hematoma

CASE 2.—An infantryman was struck in the middle third of the left leg by an artillery shell fragment on Jan. 3, 1945. Hemorrhage from the wound was slight. First-aid treatment was given but débridement was not done. The diagnosis of arteriovenous fistula of the posterior tibial vessels was made at a field hospital on the seventeenth day after injury. The patient was admitted to this hospital one month after injury. There was a to-and-fro bruit over the posterior aspect of the left leg in its middle one-third. The pulses were normal in the foot. There was no disturbance of function of the peripheral nerves. The pulse rate decreased from 116 to 96 beats per minute on compression of the fistula. Teleroentgenograms taken at a six-foot distance showed no abnormality of cardiac diameters either before or after manual occlusion of the fistula. Oxygen saturation of the femoral venous blood was 64 volumes per cent on the affected side and 46 on the normal side. On the thirty-fourth day after injury the patient complained of pain in the calf for the first time. There was obvious increase in swelling of the calf. The dorsalis pedis and posterior tibial pulses were still palpable. At operation on February 16 the specimen shown in Fig. 2 was removed. The sudden attack of pain in the calf was explained by a secondary rupture of the arteriovenous fistula. The constricting musculature of the soleus and gastrocnemius muscles accounted for the curious hourglass contour of this arteriovenous aneurysm and pulsating hematoma. The older aneurysm lay between the muscular layers of the tibialis posticus and the soleus while the communicating hematoma was encapsulated between the soleus and the gastrocnemius muscles. The lumbar sympathetic ganglia were blocked with novocain before the patient

left the operating room. Circulation of the affected extremity was ideal but the patient developed moderate contracture of the Achilles tendon and embarked for further convalescence in the United States two months after operation.

This case record calls attention to the possibility of secondary rupture of traumatic arteriovenous aneurysms. The patient was confined to bed at the time of the onset of the pain which was coincident with the secondary internal hemorrhage.

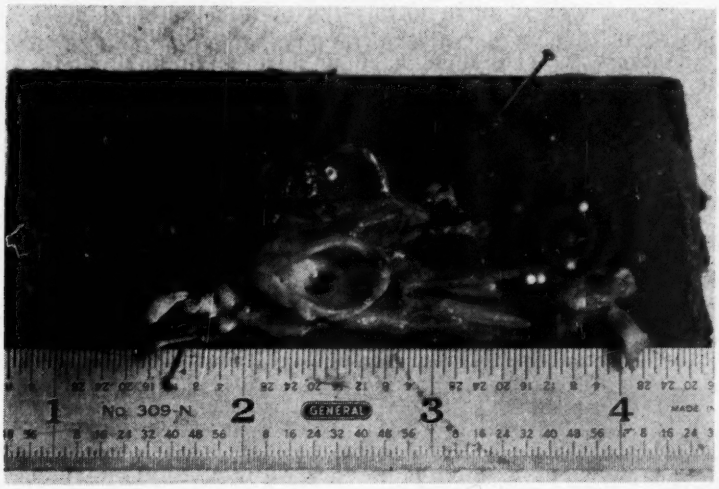
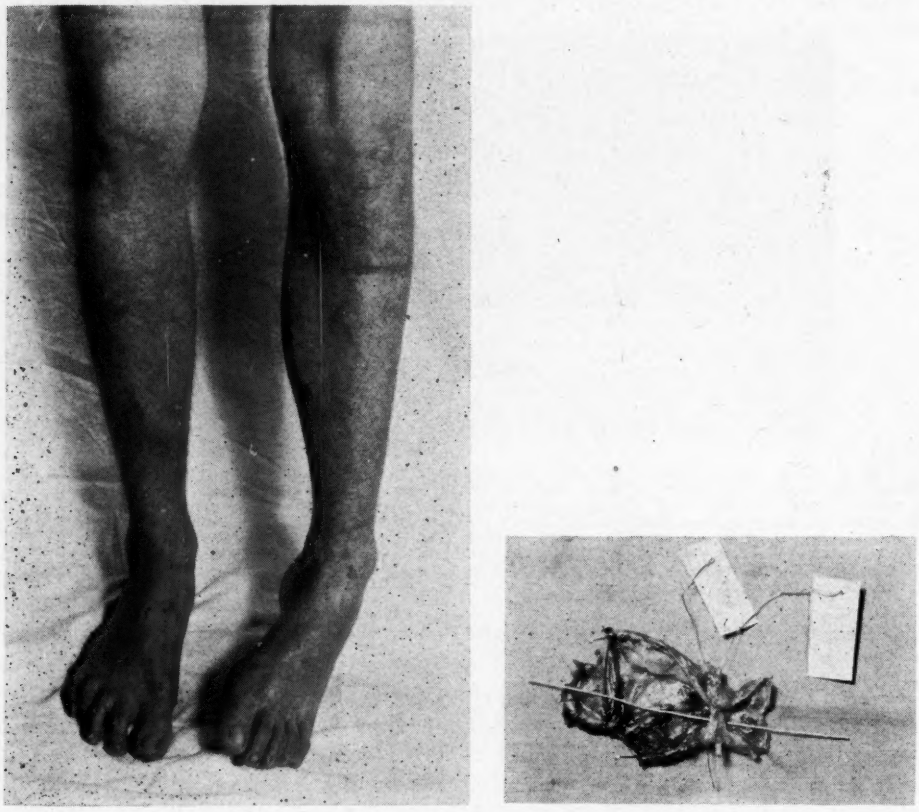


Fig. 2 (Case 2).—Photograph showing the specimen removed from patient. This is an anteriovenous aneurysm between the posterior tibial artery and several adjacent veins. The pins identify the afferent and efferent posterior tibial artery and communicating veins. The aneurysmal sac has an hourglass shape due to the formation of the original aneurysm which is immediately in communication with the vessels and the upper more recent aneurysm which developed at the time of secondary hemorrhage thirty-four days after the injury. The upper sac contained clotted blood. In the center of the lower sac, the openings into both arterial and venous channels can be seen.

Arteriovenous Fistula of the Posterior Tibial Vessels With Subsequent Rupture and the Development of Secondary Pulsating Hematoma

CASE 3.—A soldier was injured Jan. 25, 1945, by a Japanese .25 caliber bullet which entered the posterolateral aspect of the middle one-third of the left calf and made its exit on the lateral aspect of the medial one-third of the calf. There was severe hemorrhage at the time of the injury. There were no fractures or nerve injuries. He complained of pain from that time on and was admitted to this hospital on Feb. 11, 1945, with the classical signs and symptoms of arteriovenous fistula at the middle one-third of the left calf on its medial aspect. The diagnosis of the vascular lesion was established at the time of admission to this hospital. The extremity is shown in Fig. 3, *A*. There was a moderately distant to-and-fro murmur, of which the patient was conscious. The radial pulse was 85 per minute. After compression of the aneurysm it was 76. Oxygen saturation of the venous blood from the affected leg was 62 volumes per cent, and 51 from the normal side. He was kept in bed in this hospital and the popliteal artery was compressed for fifteen minutes four times each day. On March 5, while awaiting evacuation, the patient had sudden sharp pain in his calf and that area became more swollen. The dorsalis pedis and posterior tibial pulses no longer could be palpated. With the diagnosis of internal bleeding from the arteriovenous aneurysm the calf was explored on March 6. A vertical incision was made over the medial aspect of the calf posterior to the tibia. There was a large pulsating swelling 4 by 6 cm. in size, occupying a space between the soleus muscle and the tibialis posticus group. The posterior tibial

nerve was intimately adherent with this mass. The mass was almost exactly in the mid-portion of the calf. In an attempt to dissect around the aneurysm and to define the efferent and afferent arteries and veins, the thin-walled aneurysmal sac was broken into. Thick clot and fresh blood gushed forth. Tourniquet was applied and the dissection was continued. It was found that there was some shredding of the fibers of the margin of the posterior tibial nerve but that its continuity was intact. The proximal artery measured only 2 mm. in diameter and the proximal vein was 3 mm. in diameter. The distal artery and vein were of similar size. The communicating opening in the artery was 1 cm. long. The aneurysmal sac was composed of two portions, a small sac measuring 2 by 1 cm. which apparently had been formed by the limitations of the tibialis posticus muscle and a



A. *B.*

Fig. 3 (Case 3).—*A*, Photograph showing the degree of swelling of the left calf due to arteriovenous fistula between the posterior tibial artery and vein. Injury was caused by a Japanes .25 caliber bullet which entered the posterolateral aspect of the left calf in its middle one-third. The scar represents the point of exit. The fistula had formed a false aneurysm 2 cm. in diameter between the tibialis posticus and the soleus muscles. Although the patient had been kept in bed, the arteriovenous aneurysm had ruptured thirty-nine days after the original injury. Extending from the ruptured arteriovenous aneurysm three was a pulsating hematoma approximately 4 by 6 cm. in size lying in the fascial plane between the soleus and gastrocnemius muscles. The apparent foot drop is due to contracture of the tendo Achilles. There was no associated nerve injury.

B, Photograph of specimen of arteriovenous aneurysm of the posterior tibial artery and vein. The wires are inserted into the artery (right tag) and vein (left tag) which are transversely placed. The vertical probe demonstrates the arteriovenous communication. The aneurysm has an hourglass shape due to the fact that the lower, smaller sac which contained circulating blood had ruptured on the thirty-ninth day after injury to give rise to the upper thin-walled sac which was filled with clotted blood. The lower sac was limited in its development by the confines of the tibialis posticus muscle fibers while the upper, larger sac lay in the plane between the gastrocnemius and the soleus muscles.

larger more recent sac 5 by 4 cm. in size between the soleus and gastrocnemius muscles. The specimen is shown in Fig. 3, *B*. This larger sac was filled with clotted blood. Apparently it had developed when the patient experienced pain the day before operation. Quadruple ligation was done with zero black silk. The aneurysm and its adjacent vessels were excised. The abnormal arteriovenous communication was of the posterior tibial artery and vein at a point between the muscular branches and the posterior malleolar branch. The patient convalesced uneventfully except for the development of moderate contracture of the Achilles tendon. He was transferred to the United States for rest and recuperation forty-three days after operation.

The sequence of events and the pathology in this case are almost identical with those in Case 2.

Arteriovenous Aneurysm of the Brachial Vessels; Partial Paralysis of the Median Nerve

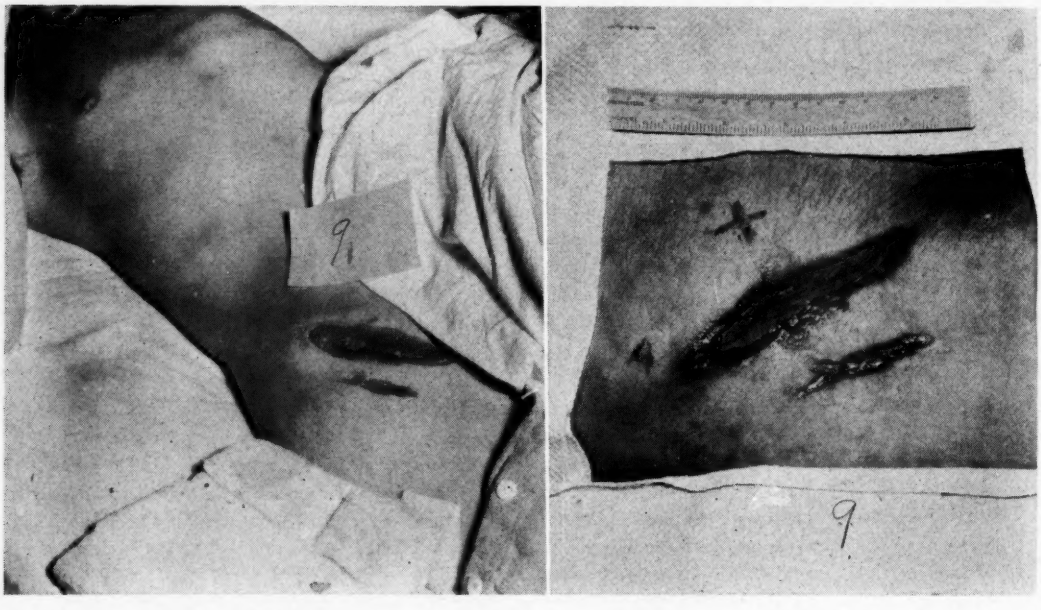
CASE 4.—A 25-year-old infantryman was struck in the lower third of the left arm by a .25 caliber Japanese rifle bullet on Feb. 24, 1945. Severe hemorrhage from the wound was treated by compression dressing. The patient was conscious of a whirring sensation in his arm just above the elbow at the time of admission to this hospital on March 24. There was a "machinery murmur" and a palpable thrill over the medial aspect of the lower third of the arm. Compression of this area did not alter the resting pulse rate of 80 per minute, the blood pressure (which was 120/80), or the cardiac diameters as demonstrated by teleroentgenograms taken at a distance of six feet. Oxygen saturation of venous blood taken from the cephalic vein on the affected side was 85 volumes per cent and on the normal side it was 45. Examination of the hand showed impairment of function of the sensory and motor components of the median nerve. There was slight secondary enlargement of the compressible swelling of the arm on April 14, forty-eight days after injury. At operation, April 16, an arteriovenous aneurysm between the brachial artery and two adjacent veins was excised. The opening in the artery was just distal to the origin of the superior ulnar collateral artery and it was not possible to save that important vascular branch. The aneurysmal dilatation extended for a distance of 3 cm. along the tract of the missile. The median nerve was firmly bound to the aneurysm by fibrous tissue. A small neuroma was excised from this nerve. The aneurysm was removed by quadruple ligation and excision. The ligated distal end of the brachial artery pulsated but the radial pulse was not palpable until twenty-four hours after operation. The circulation in the hand was excellent following operation. Novocain block of sympathetic ganglia was not necessary. Although the condition of the arm and hand were approximately normal, it was necessary to transfer the patient to the United States for convalescence from associated thoracic injury.

Arteriovenous Fistula Between the External Iliac Artery and Vein

CASE 5.—A 26-year-old infantryman was injured on Dec. 7, 1944. A .30 caliber enemy rifle bullet struck the Browning automatic rifle which he was carrying. Fragments of the bullet amputated the distal phalanx of his right ring finger and entered the tissues of the right groin. Immediate hemorrhage from the wound was slight but the patient recalls the gradual development during the next few days of a painful swelling in the groin. Within a few hours after injury he was treated at a clearing station where metallic fragments were removed from the wounds and the saphenous vein was ligated. December 24, he was admitted to the hospital, the wounds appearing as shown in Fig. 4, *A*. Thick-split grafts were applied to the wounds promptly. The appearance after grafting is shown in Fig. 4, *B*. The loud to-and-fro murmur and the thrill were maximal in intensity just above the inguinal ligament. Oxygen saturation of venous blood was 70 volumes per cent on the affected side and 45 on the normal side. There was no impairment of nutrition of the foot and the peripheral pulses were palpable though weak on the side of the affected leg. Direct compression of the fistula was reflected in a drop in pulse rate from 74 to 62 per minute and a change in blood pressure from

120/56 to 120/70. This maneuver, however, did not effect any change in cardiac diameters as shown by teleroentgenograms made at a distance of six feet. During the period while this patient was awaiting evacuation to the United States, the circulation in the fistula was occluded for ten-minute periods four times daily by direct pressure on the abdominal aorta.

In this case there was no episode of secondary bleeding and therefore no indication for operative intervention while the patient was in this hospital. Interest in this case centers on the fact that, although the fistula was a large one, still there was no sign of development of cardiac dilatation during the three and one-half month period of observation. Also, it was interesting to note that thick-split grafts afforded protection against external hemorrhage.



A. *B.*

Fig. 4 (Case 5).—*A*, Furrowed wound of the groin caused by a .30 caliber bullet. Just above the upper wound, there was a palpable thrill and a loud "machinery" murmur. Because of the danger of severe secondary hemorrhage, the wound was skin grafted promptly. *B*, Showing the appearance of the wounds after application of thick-split grafts. X marks the point of maximal intensity of the murmur.

Arteriovenous Fistula of the Femoral Vessels, Upper Third

CASE 6.—A 25-year-old infantryman was injured in the left upper anterior thigh by Japanese 90 mm. mortar shell fragments, Jan. 24, 1945. There was severe hemorrhage from the wound at the time of injury. Within two hours débridement was done at an evacuation hospital. He was admitted to this hospital on Feb. 11, 1945. The wound was healed and there were no symptoms, but swelling in the left femoral triangle was associated with the characteristic signs of arteriovenous fistula. The diagnosis was established for the first time at this hospital. Oxygen saturation tests of the blood were not done but Branham's sign was positive. The pulse rate dropped from 88 to 68 on manual compression of the fistula. Teleroentgenograms showed no cardiac enlargement and no change in cardiac dimensions after compression of the fistula. The peripheral pulses were present in both feet and nutrition of the foot on the affected side was normal. Collateral circulation was encouraged by frequent compression of the femoral artery against the head of the femur proximal to the fistula. There

was no secondary swelling and no other indication for operative intervention at this station. The soldier was transferred to the United States for further care thirty-five days after admission.

Arteriovenous Fistula of Internal Carotid Artery and Jugular Vein

CASE 7.—A 23-year-old infantryman was struck by an enemy shell fragment in the right side of the neck on Jan. 30, 1945. The shell fragment entered the neck just anterior to the upper third of the sternocleidomastoid muscle and lodged lateral to the body of the third cervical vertebra. There was significant hemorrhage from the wound. Emergency care was given at a field hospital where the diagnosis of arteriovenous fistula was made one day after injury. The characteristic to-and-fro murmur was heard over the upper portion of the anterior cervical triangle. Compression of the fistula was reflected by a drop in pulse rate from 88 to 84 and a rise in blood pressure from 120/80 to 130/85. Teleroentgenograms taken at a six-foot distance showed no cardiac dilatation and there was no variation in cardiac dimensions after manual obliteration of the fistula. The patient was conscious of a buzzing sensation in the right side of the neck. The optic fundi were normal. There was no venous dilatation. There were no episodes of pain or secondary swelling and no indication presented for early surgical intervention. The patient was transferred to the United States for further care.

Arteriovenous Fistula of the Femoral Vessels in Their Middle Third

CASE 8.—A 28-year-old private in a chemical battalion suffered multiple wounds of the right thigh from Japanese artillery shell fragments, Jan. 20, 1945. There was mild hemorrhage from the wounds. Early treatment consisting of sulfanilamide dressings was carried out at a clearing station within one hour after injury. The diagnosis of arteriovenous fistula was made on a hospital ship enroute to this base. On admission to this hospital on February 25, examination showed that the wounds were healed. The bruit and murmur characteristic of arteriovenous fistula were present over Hunter's canal in the middle third of the thigh. There was no significant dilatation of the veins of the affected leg. Branham's sign was positive; the pulse rate dropped from 96 to 80 on compression of the fistula. There was no cardiac dilatation as measured by teleroentgenograms taken at a distance of six feet and compression of the fistula did not cause any change in cardiac dimensions. The patient was given regular treatments consisting of compression of the femoral artery against the head of the femur for twenty minutes every four hours until April 18, the date on which he embarked for the United States by hospital ship.

In this case there was no sign of secondary rupture of the fistula and no indication for early surgical intervention.

Arteriovenous Fistula of the Femoral Vessels, Middle Third

CASE 9.—A 25-year-old sergeant, attached to a tank battalion, was wounded in the right thigh by fragments of a Japanese hand grenade on Feb. 7, 1945. There was severe hemorrhage from the wound of entrance over the anterior aspect, middle third of the right thigh. He was treated at an evacuation hospital and transferred to this base via hospital ship. The diagnosis of arteriovenous fistula was made for the first time on admission to this hospital, February 27. The patient was conscious of a buzzing in the thigh and complained of constant mild pain in the thigh. Evidence of nerve damage existed in that there was loss of dorsiflexion of the great toe. Branham's sign was positive, the pulse rate dropping from 92 to 80 after compression of the fistula. Regular vascular exercises to promote collateral circulation were given as in Cases 7 and 8, and the patient embarked via hospital ship for the United States on April 18.

Arteriovenous Fistula of the Femoral Vessels, Middle Third; Division of the Saphenous Nerve

CASE 10.—A corporal in the Philippine Army was wounded by artillery shell fire on Oct. 23, 1944. Information regarding treatment prior to admission to this hospital was incomplete,

the records revealing only that the wounds were dressed and sulfadiazine was administered. On November 2, physical examination showed that the wound of entrance was on the medial aspect, middle one-third of the right thigh, and that the wound of exit was on the lateral aspect of the thigh at the same level. There was flexion contracture of the knee as shown in Fig. 5. Within a few days the wounds were healed. There was a palpable thrill and a loud to-and-fro murmur over the medial aspect of the middle third of the thigh. Compression of the femoral artery against the head of the femur caused the bruit to disappear. Compression of the

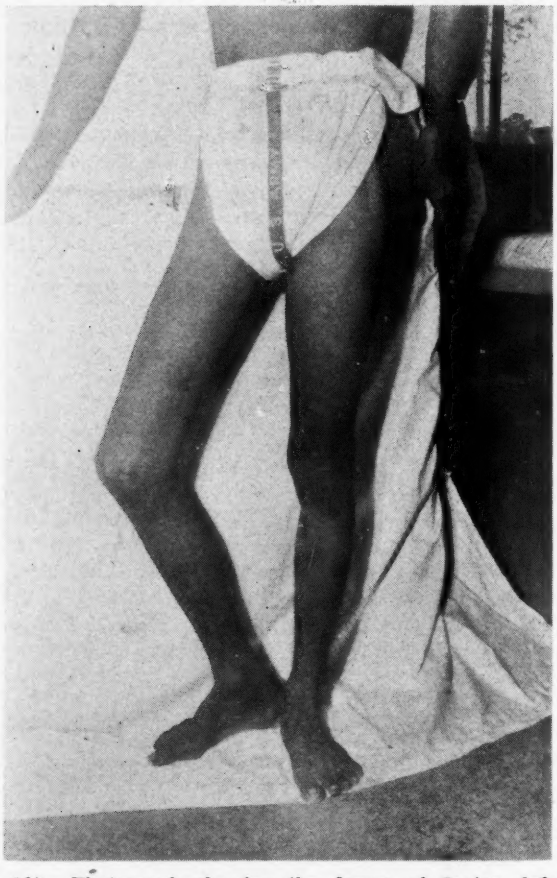


Fig. 5 (Case 10).—Photograph showing the degree of flexion deformity of the knee caused by arteriovenous fistula of the femoral artery and vein in their middle thirds. The patient is holding the right knee in full active extension.

fistula itself was followed by a drop in pulse rate from 96 to 80 per minute and by a rise in blood pressure from 102/60 to 112/62. However, teleroentgenograms taken at a distance of six feet after compression of the fistula showed no difference in the measurements of the cardiac shadows. There was no cardiac dilatation. The veins of the lower leg were distended. The popliteal, dorsalis pedis, and posterior tibial pulses were palpable. For thirteen weeks prior to operation, the patient was treated by frequent compression of the femoral artery against the head of the femur in order to promote the development of collateral circulation. The patient was necessarily held in this hospital pending orders from the Philippine Army for his transfer. At operation, January 31, the fistula was found to have developed between the femoral artery and vein at a point just proximal to the highest genicular artery. The fistula had undergone aneurysmal dilatation. It measured 2.7 cm. in transverse diameter.

There were a number of collateral veins which communicated with it. The continuity of the saphenous nerve had been interrupted by the missile and the frayed ends of the nerve were adherent to the fibrous sac of the aneurysm. Quadruple ligation and excision of the aneurysm were done. Incision of the specimen showed that in it there were several loose clots. The saphenous nerve was sutured. Novocain block of the lumbar ganglia on the affected side was done. The circulation in the foot was satisfactory after operation but on the fifth post-operative day the patient died from a massive pulmonary embolus. Post-mortem examination showed that there was a thrombus in the femoral vein proximal to the point at which it had been ligated.

In only two of these cases was there associated impairment of peripheral nerve function. One of these was the fistula of the brachial vessels which showed partial loss of motor and sensory functions of the median and ulnar nerves. In another case there was complete division of the saphenous nerve in association with an arteriovenous fistula of the femoral vessels. This is of interest in view of the fact that nerve injuries were more frequent in the patients with false aneurysms in this series. Studies on the effects of the peripheral fistula on the vascular system showed that Branham's sign was positive in nine of the ten patients. In all of the ten there was persistent tachycardia ranging from a pulse rate of 80 per minute to 110 per minute. In the patients with femoral arteriovenous fistula the average drop in pulse rate following compression of the fistula was 16 beats per minute. In those with posterior tibial arteriovenous fistula the corresponding average was 12. In the one patient with external iliac arteriovenous fistula the drop in pulse rate on compression of the fistula was 12 per minute. Compression of the fistula of the brachial vessels was not reflected in relative bradycardia. These observations do not contribute any evidence to support the teaching that the size of the fistula and its proximity to the heart are in relationship to the degree of tachycardia present and to the degree of bradycardia which follows compression of the fistula. Moreover, at the time of admission to this hospital (an average of twenty-one days after injuries were sustained) none of these patients showed cardiac enlargement or variation of cardiac diameters as measured by teleroentgenograms taken at a distance of six feet before and after compression of the fistulas. It is clear from this evidence that the cardiac dilatation which is referred to often as an invariable secondary effect of arteriovenous fistula is not present soon after the development of these vascular abnormalities. The impression obtains that this complication develops slowly and progressively secondary to persistently increased volume flow of blood through the heart. Pain in the involved extremity was a symptom in four cases. Flexion deformity of a neighboring joint was a significant finding in only one of these ten cases. This observation is of interest in view of the fact that of the ten patients with false aneurysms, five developed flexion contractures soon after injury. The characteristic "machinery murmur" or "to-and-fro bruit" was present on auscultation over the involved area in all ten cases of abnormal arteriovenous communication. In only four cases was the patient conscious of a thrill over the involved area. In three of these patients there was an episode of increasing pain over the involved area with secondary increase in regional swelling. The underlying pathology in these cases proved to

be an hourglass type of aneurysm due to secondary rupture of the aneurysmal arteriovenous communication, the newly formed hematoma being limited in its development by the fascial sheaths of another anatomic plane. In five of the ten patients in whom specimens of venous blood were taken from the involved extremity and from its fellow there was increased oxygen saturation on the involved side. In all patients attention was directed toward the development of collateral circulation by frequent compression of the artery proximal to the fistula. In three cases it was necessary to operate because of the complication of secondary swelling. In a fourth case a small fistula was excised by quadruple ligation of the lower posterior tibial vessels and the patient was returned to duty. The fifth patient, who was operated upon, was a Philippine soldier who spent three months at this station awaiting transportation to a hospital in the Philippine Islands. During this period collateral circulation was established by regular periods of compression of the artery proximal to the fistula. The fistula then was excised. There were no peripheral vascular complications following surgical excision of the fistulas in these five patients. In two of them, however, contracture of the Achilles tendon developed following excision of fistula of the posterior tibial vessels in their lower one-third. Of these ten patients with arteriovenous fistula, five were transferred to the United States for operative treatment and five were operated upon in this general hospital without peripheral circulatory complications but with one death due to pulmonary embolus. The average elapse of time between dates of injury and operation was sixty-one days. One of these soldiers was returned to duty and two others might have been returned to duty except for the presence of associated injuries which required a prolonged period of convalescence.

FALSE ANEURYSM AND PULSATING HEMATOMA

Since false aneurysm and pulsating hematoma are complications secondary to incomplete lacerations of arteries, these cases have been grouped together in this presentation. There were ten cases in all. In three there were well-developed false aneurysms which had ruptured secondarily with resultant formation of a secondary pulsating hematoma. Four were examples of false aneurysms with well-developed fibrous sacs containing circulating blood. In three patients with pulsating hematoma, the clot had plugged effectively the tangential tear of the artery and had not yet undergone liquefaction.

The surgical management of these patients presented a variety of problems. While awaiting the development of collateral circulation the indication for operation presented when sudden pain and increased swelling about the vascular lesion indicated that a secondary hemorrhage into the tissues had taken place. This occurred in five of the ten cases. In three of these the swelling was of such degree that pulses peripheral to the lesions were no longer palpable. In these cases operation was performed as an emergency procedure. In a sixth case, brisk hemorrhage from a granulating wound overlying a false aneurysm necessitated exploration. Progressive dysfunction of involved peripheral nerves constituted the indication for operation in three additional patients. In the tenth case a

small aneurysm of the brachial artery was discovered during operation as neurolysis of the median nerve was being done.

Five of these incomplete arterial lacerations were caused by small artillery shell fragments. Two were caused by .25 caliber Japanese rifle bullets, two by .31 caliber Japanese machine gun bullets, and one by a .50 caliber machine gun bullet. In all cases the missiles were small. Immediate hemorrhage from the wound was mild in nine patients and severe in one. The diagnosis was made prior to admission to this hospital in only one case. This is explained easily since it has been our observation that the systolic bruit characteristic of pulsating hematoma and false aneurysm may not be present in the early days following injury. It has been observed that the true pulsating hematomas, those in which the clot has not liquefied, give rise to a bruit which is only faintly audible. As the false aneurysmal sac forms and the clot liquefies, the bruit becomes more intense. In all of these cases of false aneurysm and pulsating hematoma, pressure on the bell of the stethoscope caused the bruit to disappear and the distal pulses to be no longer palpable. The average number of days which elapsed between injury and diagnosis was seventeen.

Five of these vascular lesions were of the brachial artery, one was in the second portion of the axillary artery, one was of the radial artery, one was of the posterior tibial artery, one was of a muscular branch of the femoral artery, and the tenth aneurysm arose from the ulnar artery.

CASE REPORTS

False Aneurysm of the Radial Artery With Impairment of Function of the Median Nerve

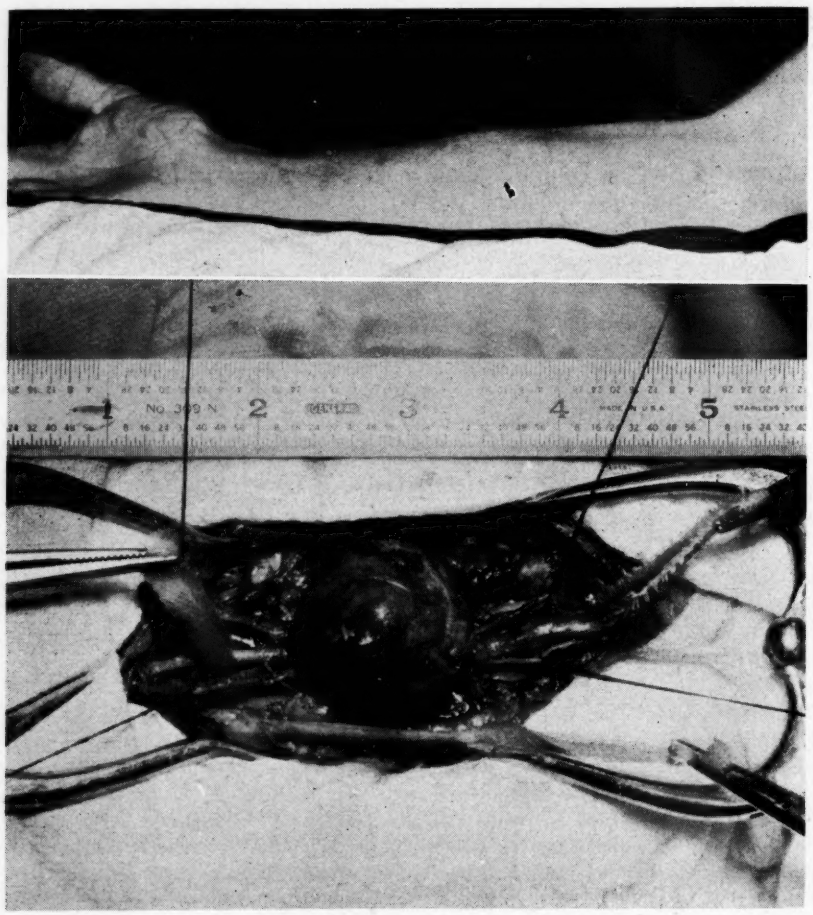
CASE 11.—A 19-year-old infantryman sustained a penetrating wound of the left forearm from an enemy hand grenade fragment on Dec. 17, 1944. Débridement was done at a clearing station and the soldier was admitted to this hospital Jan. 7, 1945, at which time the diagnosis of false aneurysm was made. Painful swelling had been noted since the second day after injury. There was an expansile, pulsating swelling 4 cm. in diameter over the radial side of the middle third of the flexor surface of the right forearm. The arm is shown in Fig. 6, *A*. There was a systolic bruit over this swelling and pressure on it caused obliteration of the radial pulse. There was hyperesthesia over the area of the hand supplied by the median nerve and movements of the fingers were coarse. For this reason the lesion was exposed at operation on Jan. 24. The median nerve was embedded in fibrous tissue around the false aneurysm which was 2.5 cm. in diameter. A photograph was taken at the operating table (Fig. 6, *B*). It was noted that the artery measured only 2 mm. in diameter proximal to the aneurysm but was 3.5 mm. in diameter distal to the aneurysm. Despite the thin fibrous coat which constituted the aneurysmal sac, it was possible to dissect it out completely and to excise it with a segment of artery. The concomitant vein was ligated and divided. Examination of the specimen showed that the rent in the artery was 3 mm. in diameter. The sac contained a central clot and free blood peripherally. There were no striae lining the false aneurysmal sac as is seen in similar lesions which have been present for a longer time. Following excision of the lesion, the radial pulse was palpable at the wrist. The soldier was given intensive physical therapy to the hand and was returned to duty at his own request on May 1, with full function of the hand.

False Aneurysm of the Brachial Artery With Compression of the Median Nerve

CASE 12.—A 34-year-old infantryman was struck in the left arm on Oct. 25, 1944, by a .25 caliber Japanese rifle bullet which entered the anteromedial surface of the arm and made

its exit from the posteromedial surface. There was an expansile, pulsating swelling over the medial aspect of the middle one-third of the left arm and a fairly loud systolic bruit could be heard over this area. Pressure on this swelling caused obliteration of the pulses distally. The patient complained of pain at the site and there was limitation of extension (20 degrees) of the elbow. Blood pressure taken at the right arm was 115/70, while on the left it was 70/40. Because of the progressive anesthesia of the palm, the patient was operated upon December 15. The median nerve was found to be firmly adherent to the fibrous mass which represented the false aneurysm. The nerve was dissected away and was found to be intact. The aneurysm, which was 4 cm. in diameter, arose from the brachial artery just distal to the point at which the superior ulnar collateral branch arises. By careful dissection it was possible to preserve this branch as the involved segment of brachial artery with its aneurysm was excised. Following excision the radial pulse was faintly palpable. The concomitant vein was ligated and divided. Novocain block of the cervical sympathetic ganglia was done. The patient made an uneventful recovery and embarked for the United States on Dec. 30, 1944.

A.



B.

Fig. 6 (Case 11).—*A*, Swelling of the flexor surface of the forearm due to false aneurysm of the radial artery. *B*, Photograph taken after dissection of the vascular lesion at operation. The gauze tape on the left supports the radial artery proximal to the false aneurysm while that on the right supports the same artery distally. Note the variation in diameter of the artery proximal to and distal to the aneurysm. The lowermost gauze tape retracts the median nerve while the silk sutures are placed around adjacent veins.

False Aneurysm of the Brachial Artery in Association With Median Nerve Paralysis

CASE 13.—A 25-year-old soldier had been struck in the left arm by artillery shell fragments on Feb. 28, 1945. Examination showed almost complete paralysis of the median nerve. At exploratory operation it was found that the median nerve was adherent to a pulsating mass which projected from the brachial artery. This aneurysm was only 4 mm. in diameter. The adventitia of the artery was successfully plicated over the aneurysmal bulge with five silk sutures. A small neuroma was excised from the median nerve. The patient was transferred to the United States on April 18, 1945. Function of the hand had improved remarkably.

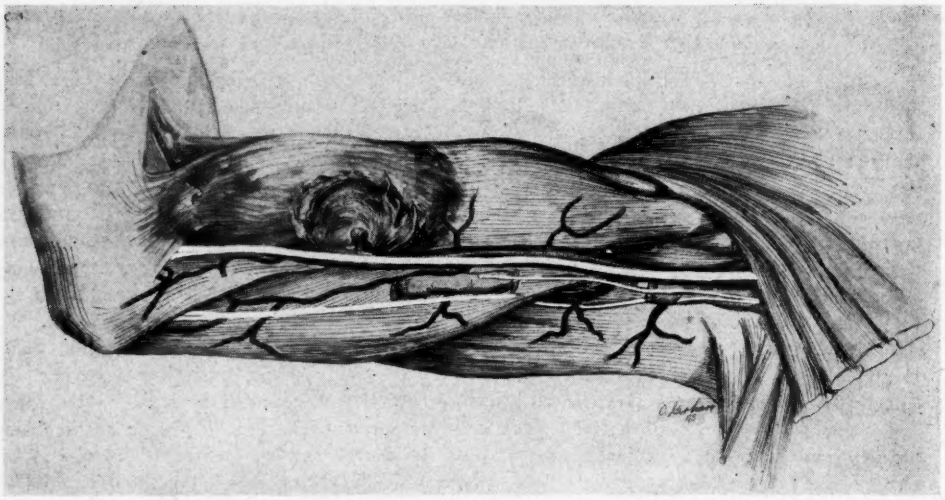
False Aneurysm of a Muscular Branch of the Femoral Artery Causing Exsanguinating External Hemorrhage

CASE 14.—An infantryman was injured in the left leg by enemy shell fragments on March 7, 1944. There was a deep wound of the soft tissues of the anteromedial aspect of the left thigh and there were compound fractures of the tibia and fibula on the same side. Débridement of the wounds was done at a medical regiment. It was stated in the record that at that time "a large clot was disturbed in the wound of the upper thigh causing profuse bleeding." The patient was admitted to this hospital with the leg in a plaster cast March 16. Inspection of the wounds of the lower leg showed that it was exuding gas bubbles and foul-smelling pus. *Clostridium welchii* was recovered. Incision and drainage were instituted. The wound of the upper thigh was not contaminated with *Cl. welchii*. On March 20 there was an exsanguinating hemorrhage from the wound of the upper thigh. Emergency exploration revealed that the source of the hemorrhage was a ruptured false aneurysm which arose from the muscular branch of the femoral artery which supplies the vastus medialis. The aneurysm was 2 cm. in diameter. The artery and the aneurysm were excised. The patient made an uneventful convalescence from both conditions and was transferred to another hospital on May 10, 1944.

False Aneurysm of the Brachial Artery With Secondary Rupture and Formation of Adjacent Pulsating Hematoma; Partial Paralysis of the Median Nerve

CASE 15.—A 27-year-old infantryman was struck in the left arm by mortar shell fragments while on a landing barge, Oct. 20, 1944. There was only slight hemorrhage from the wound. The soldier was admitted to this hospital on October 25. Examination showed that the left elbow was held at right angle flexion and there was a tense, expansile swelling of the lower third of the arm. A systolic bruit could be heard over this area. The degree of swelling is shown in Fig. 7, *A*. There were signs of impairment of function of the median nerve. The patient was kept in bed with the left arm in a sling. Despite these precautionary measures the patient experienced severe pain in the arm on November 10, twenty-one days after injury. Examination showed that the swelling of the lower arm had increased so that the tissues were quite tense. The angle of flexion at the elbow now had become acute. The radial and ulnar pulses were no longer present. The bruit had diminished in intensity. Ecchymosis of the tissues of the arm developed. At operation the dissection was made difficult by reason of the fact that, as the brachial artery was identified proximal to the lesion, the entire vascular tree of the arm went into vasospasm. The fascial sheath of the biceps brachii was distended by a tense mass and the tissues of the region were ecchymotic. The median nerve was adherent to this mass, which was limited anteriorly by the fascia of the biceps and inferiorly by the lacertus fibrosus. With gauze tapes securely placed around the artery proximally and distally, a tense hematoma measuring 8 by 6 cm. in size was broken into. Sixty cubic centimeters of clotted blood escaped, exposing a false aneurysmal sac 4 cm. in diameter. This had arisen from the brachial artery between the points at which the superior and the inferior ulnar collateral arteries arise. The opening into the brachial artery was 1 cm. in its greatest diameter. The pathologic picture is demonstrated in the artists's sketch shown in Fig. 7, *B*. This case would have been an excellent one for the Matas endo-

A.



B.

Fig. 7 (Case 15). *A*, Photograph showing the swelling of the lower third of the arm due to false aneurysm. The patient is holding the elbow in full active extension. This photograph was taken before the development of secondary swelling.

B, Artist's sketch showing the false aneurysm of the brachial artery which had ruptured to form a pulsating hematoma limited in its size by the fascial sheaths of the biceps brachii and the lacertus fibrosus. Note that the false aneurysm arises from the artery at a point midway between the points of origin of the superior and inferior ulnar collateral branches. The sac of the false aneurysm although thin was well formed and its lining showed circular striations, an effect of the whirlpool of blood within it.

aneurysmorrhaphy but since heparin was not available, the entire arterial segment between the superior ulnar collateral and the inferior ulnar collateral was excised. The concomitant vein was ligated and divided. At the close of the operation, the hand was cold though its color was good. Injection of novocain into the stellate ganglion was followed by return of warmth to the hand. The patient made an uneventful convalescence and was transferred to the United States on Dec. 16, 1944.

The interesting feature of this case was that the secondary hemorrhage from rupture of the false aneurysm occurred while the patient was at rest in bed with the affected arm in a sling.

False Aneurysm of the Brachial Artery With Associated Paralysis of the Median Nerve

CASE 16.—A 19-year-old paratrooper was wounded in the right arm by a fragment of mortar shell, Feb. 5, 1945. The missile entered the medial aspect of the lower third of the arm and lodged in the muscular tissue of the biceps. There was only slight hemorrhage from the wound of entrance. Early treatment was given at a station hospital. The diagnosis of pulsating hematoma was made at this hospital at the time of admission sixteen days after injury. During the next three days the systolic bruit over the lower arm became more intense and the diagnosis was changed to false aneurysm. There was almost complete paralysis of the median nerve. The radial pulse was palpable. The resting pulse rate, which had been 76 per minute, rose sharply to 90 on February 27 as the patient complained of constant pain in the lower arm. Fig. 8 is the photograph taken on that date. The bruit became less intense

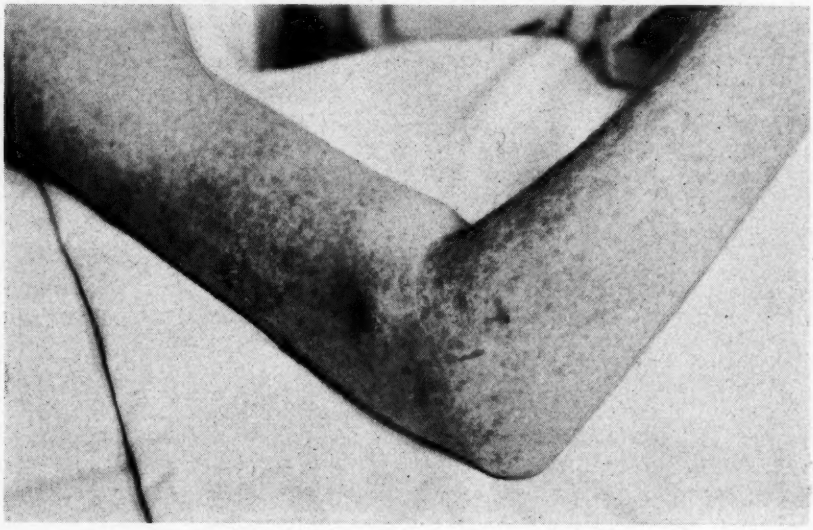


Fig. 8 (Case 16).—False aneurysm of the lower third of the brachial artery with secondary swelling due to second episode of hemorrhage. The elbow is held in right-angle flexion. Note the bulge of the granulating wound at the point of entrance of the shell fragment.

following this new episode of pain. The granulating wound at the point of entrance of the missile bulged progressively and flexion deformity of the elbow became more marked during the next forty-eight hours. Because the radial pulse was obliterated by the swelling it was necessary to explore the arm at operation on March 1. The pulsating mass proved to be a false aneurysm of the brachial artery which contained four ounces of blood and blood clot. After securing the artery proximally and distally with tape, the thin-walled sac was entered. The aperture in the brachial artery was a tangential opening 2.5 mm. in length and 1 mm. in width. As in Case 15, the tear was in the segment of brachial artery between the

superior and inferior ulnar collateral branches. This segment of artery was excised and a neurolysis of the median nerve was done. The concomitant vein was ligated and divided. The patient was transferred to a hospital in the United States, April 1, 1945, and made an uneventful canvalescence.

Interest centers in the parallelism between the sequence of events in this case and in Case 15. In the latter, the secondary rupture of a false aneurysm of the same artery at the same level had occurred twenty-one days after injury while the patient was at rest in bed with the arm supported in a sling. In this case the circumstances were identical except that the episode of secondary hemorrhage occurred on the twenty-second day after injury.

Pulsating Hematoma of the Brachial Artery, With Rupture and Formation of Secondary Pulsating Hematoma; Partial Paralysis of Median Nerve

CASE 17.—A 27-year-old infantryman presented history and physical findings which were very similar to those in Cases 15 and 16. The injury was caused by a .31 caliber enemy machine gun bullet on Jan. 29, 1945. The missile entered the medial aspect of the lower third of the arm and lodged in the subcutaneous tissue of the lateral aspect of the arm. There was a faint systolic bruit over the swelling of the lower arm which is shown in Fig. 9. Here

Fig. 9 (Case 17).—Photograph showing swelling of the antecubital fossa due to pulsating hematoma arising from the lowermost segment of the brachial artery. Note the dimpled scar on the medial aspect of the arm. This represents the point of entrance of the missile. The elbow is limited in extension to an agle of 110 degrees.

again there were signs of sensory and motor dysfunction of the median nerve and the angle of greatest extension at the elbow was 110 degrees. Compression of the pulsating, firm mass caused obliteration of the radial and ulnar pulses. This patient was conscious of the pulsation in the region of the elbow. On February 23, twenty-five days after injury, the patient complained of pain and increased swelling over the lower arm. The pulse rate jumped from 72 to 88. This occurred while the patient was at rest in bed. The swelling increased progressively until February 26, when, because of the tenseness of the swelling and sudden obliteration of the radial and ulnar pulses, it was necessary to explore the arm. At opera-

tion a double pulsating hematoma was exposed. Approximately one-half of the wall of the artery had been destroyed through a distance of 2 cm. The distal margin of the tear was only 4 mm. proximal to the bifurcation of the brachial artery into its radial and ulnar branches. A recent blood clot was broken into and two ounces of tightly packed clot were removed from a thin fibrous cavity limited by the muscle planes of the lacertus fibrosus and the biceps brachii. In the floor of this fibrous cavity there was a defect 1 cm. in diameter. This was plugged by organized clot around which bright red blood escaped. This cavity was opened into and found to measure 5 by 3 cm. in size. One and one-half ounces of organized blood clot were removed exposing the tear in the brachial artery as described previously. The involved segment of artery was excised and neurolysis of the adherent median nerve was done. The concomitant vein was ligated and divided. At the time of transfer to a hospital in the United States on March 21, the wound was healed and there was some evidence of returning function of the median nerve although the contracture of the elbow was still present.

The striking similarity of this case report to that of Cases 15 and 16 emphasizes the great danger of secondary rupture of false aneurysms. In all three of these cases the secondary hemorrhage occurred between the twenty-first and twenty-fifth day after injury. In all three there was danger of gangrene of the arm following the episodes of secondary hemorrhage.

Pulsating Hematoma of the Posterior Tibial Artery With Rupture and Formation of Secondary Hematoma; Paralysis of the Posterior Tibial Nerve

CASE 18.—A 21-year-old infantryman was struck by a missile from an enemy .31 caliber machine gun in the left leg below the knee on March 27, 1945. The missile entered the anterolateral aspect of the leg just inferior to and anterior to the head of the fibula. Its course was posteriorly and medially to lodge in the subcutaneous tissues of the posteromedial aspect of the upper third of the leg. At a battalion aid station, the foreign body was removed through an incision posteriorly. The patient was given sulfanilamide dressings and penicillin therapy was started. There was only slight hemorrhage from the wound of entrance. Débridement was not done. The diagnosis of pulsating hematoma was not made until April 16, the date of admission to this hospital. At that time the wound of entrance presented a sinus 5 cm. deep. The incision for removal of the foreign body had healed. There was a pulsating swelling which seemed to be in the muscles of the calf and also between the tibia and fibula. A distant systolic bruit could be heard over the posterior aspect of the calf. The dorsalis pedis and posterior tibial pulses were of full volume. There was anesthesia of the sole of the foot and the patient was unable to plantar flex the foot or toes. Attention was directed toward healing of the wound of entrance. The patient was kept at rest in bed. Gradually the wound of entrance filled in with granulation tissue and epithelized. On May 15, a medical officer, using a hemostat, inadvertently explored the thinly epithelized area representing the point of entrance of the missile. The patient suddenly complained of increased swelling in the calf and of pain about this area. There was blood tinged drainage from the thin epithelium over the point of entrance. Appearance at this time is shown in Fig. 10. Following this episode the dorsalis pedis and posterior tibial pulses were absent. Because of the danger of gangrene of the leg, surgical exploration was carried out on May 16. Consideration was given to the fact that the pulsating hematoma might have had its origin from partial tears of both the anterior and the posterior tibial arteries. The path of the missile was such that both vessels might have been damaged. The bruit was heard only over the posterior aspect of the calf while the maximal swelling was on the anterolateral aspect of the calf anterior to the head of the fibula at which point the missile had entered. The popliteal space and the calf were explored through an L-shaped incision. The two heads of the gastrocnemius were separated and the soleus was divided vertically. The popliteal artery and vein were identified. The posterior tibial artery was identified and secured with a gauze tape above and below the expansile, pulsating swelling which was between the soleus and the tibialis

posticus muscles. As the posterior tibial nerve was dissected free from the fibrous wall of the hematoma, it was found that two-thirds of its diameter had been destroyed through a distance of 2 cm. The hematoma was then evacuated. In this case the old blood clot could not be distinguished from the more recent formation. The clot was tightly packed in a cavity between the gastrocnemius and soleus muscles. It extended along the tract of the missile,

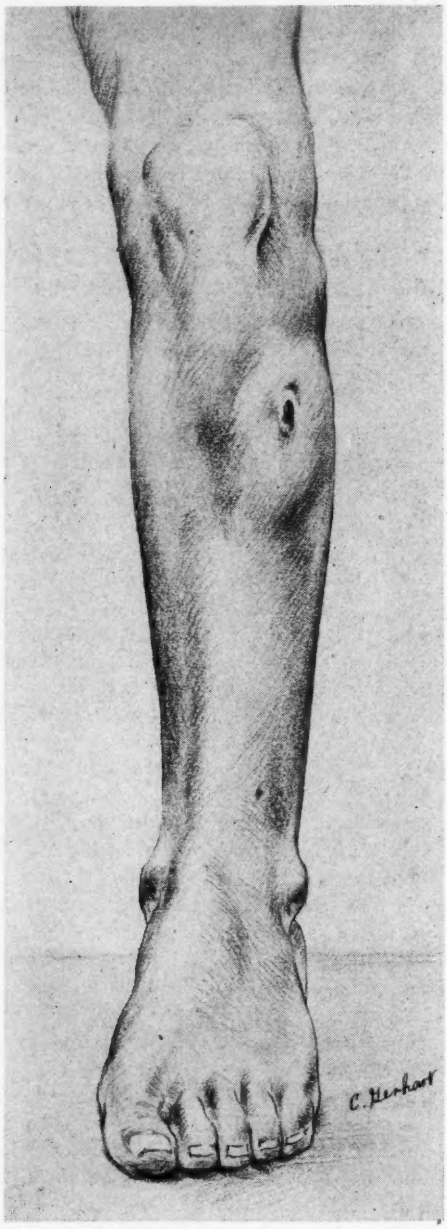


Fig. 10 (Case 18).—Artist's sketch showing the swelling of the upper leg due to pulsating hematoma secondary to injury of the posterior tibial artery. In this case there was a spontaneous secondary hemorrhage on the nineteenth day after injury. The hematoma expanded in the direction of the path of the missile causing the appearance of blood-tinged drainage from the thin epithelium over the point of entrance of the missile.

through the interosseous membrane to cause swelling near the point of entrance of the missile anteriorly. The cavity measured approximately 6 by 6 by 7 cm. in size, and from it seven ounces of clotted blood were removed. The injury to the posterior tibial artery presented as a tangential tear with destruction of one-half of the substance of the wall through a distance of 1 cm. between the retracted margins of the vessel. The involved segment of artery was excised. The posterior tibial vein was ligated and divided. The wound was closed without drainage. Following operation the dorsalis pedis pulse was present but the posterior tibial pulse was absent. Novocain block of the lumbar sympathetic ganglia on the affected side was done. The color and the circulation of the foot were normal on June 5, when the patient was transferred to the United States.

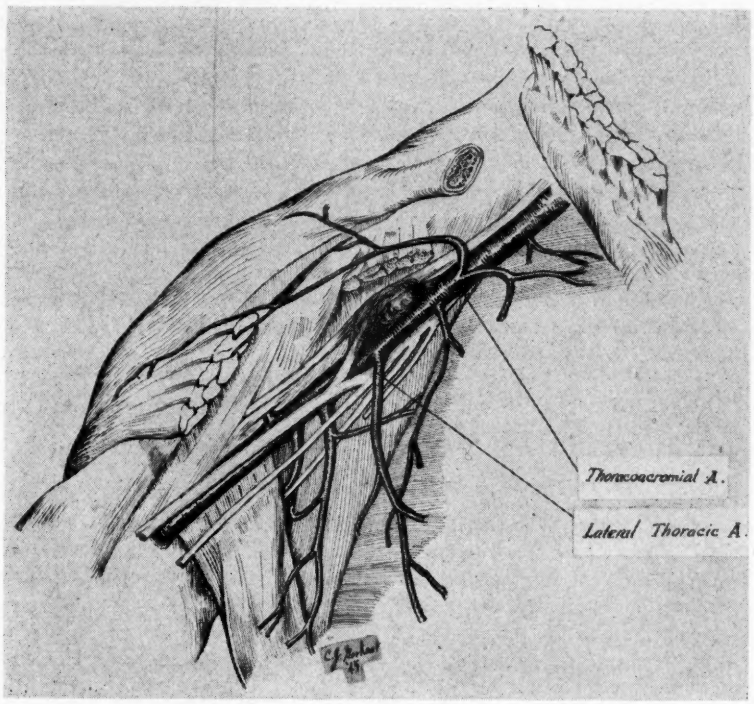


Fig. 11 (Case 19).—Sketch showing the location of this pulsating hematoma due to a partial tear of the second portion of the axillary artery. There were signs of incomplete paralysis of the brachial plexus. The extent of the hematoma was limited by the constricting brachial plexus. It was possible in this case to preserve the lateral thoracic and thoracoacromial branches at the time of excision of the involved segment of axillary artery.

Pulsating Hematoma of the Second Portion of the Axillary Artery; Partial Paralysis of the Brachial Plexus

CASE 19.—A 19-year-old infantryman was struck in the left shoulder posteriorly by a .25 caliber Japanese sniper's bullet on Oct. 20, 1944. The missile made its exit from a point just inferior to the lateral third of the left clavicle. His complaints were of inability to extend his wrist and of weakness of the forearm musculature. There was no primary débridement of the wounds. The diagnosis of pulsating hematoma was established at the time of admission to this hospital, October 27. There was fullness in the left infraclavicular area and a faint systolic murmur could be heard at this joint. The brachial, radial, and ulnar pulses were palpable and equal on the two sides. The blood pressure was recorded at 135/80 and was equal in the two arms. Pressure on the infraclavicular area caused obliteration of the brachial, radial, and ulnar pulses. There was an irregular area of anesthesia over the

dorsum of the hand. A definite wrist drop was present. Vascular collateral was encouraged by compressing the subclavian artery against the first rib at regular intervals each day. Because of the persistent paralysis, the infraclavicular and axillary regions were explored through a curvilinear incision on December 13. The clavicle was divided and the two ends were retracted as shown in Fig. 11. Exposure of the brachial plexus revealed that there was dense scar involving all three cords just proximal to the point at which the lateral and median cords combine to form the median nerve. Over this area there was a mass of degenerated fat approximately 2 by 3 cm. in size. As the scar tissue was dissected away from the components of the brachial plexus, it became apparent that this was a pulsating hematoma which had developed from a tear in the second portion of the axillary artery. The hematoma had been limited in its extension by the areolar tissue of the neurovascular bundle. As the dissection proceeded it was determined that there was no evidence of direct damage to any of the cords of the plexus but that the lateral cord had been flattened out by pressure from the pulsating hematoma. The axillary artery was secured with a gauze tape just proximal to the point where the lateral thoracic artery branches off. An ovoid blood clot 2 cm. in diameter and with dense fibrous reaction around it was removed from its position surrounding the second portion of the axillary artery and surrounded by the cords of the brachial plexus. The opening in the wall of the axillary artery measured only 3 cm. The segment of axillary artery which was between the lateral thoracic and the thoraco-acromial branches was excised. The proximal arterial stump pulsated following ligation but the distal end did not. In the closure of the wound the ends of the clavicle were approximated with wire. The cervical sympathetic ganglia were blocked with novocain and the circulation in the hand was adequate from that time on. The patient was transferred to the United States on December 29.

Interest in this case centered on the manner in which the constriction of the fibers of the neurovascular bundle enclosing the brachial plexus and the axillary artery effected limitation of extension of the pulsating hematoma.

Pulsating Hematoma of the Ulnar Artery

CASE 20.—A 21-year-old aviator was injured in the left wrist by a .50 caliber machine gun bullet while he was repairing the weapon on April 6, 1945. Examination May 11 showed a pulsating swelling 3 cm. in diameter over the flexor surface of the ulnar side of the forearm just proximal to the ulnar styloid process. There was a faint systolic bruit over the mass. There was numbness and tingling in the little and ring fingers but motor power of the ulnar nerve was not impaired. At operation, May 11, it was found that the ulnar nerve was adherent to a fibrous mass 3 cm. in diameter which enclosed clotted blood. This had developed from a partial tear of the ulnar artery at a point just proximal to the volar carpal ligament. The opening in the artery was 3 mm. in diameter. Following excision of the involved segment of ulnar artery, both the proximal and distal stumps pulsated. The adjacent vein was ligated. At no time was the circulation of the hand impaired. This soldier made an uneventful convalescence.

It is considered significant that regional peripheral nerves were involved in the fibrous reaction about the vascular lesion in all ten cases. Moreover, there were peripheral signs of motor and sensory dysfunction of the involved nerves in all of the cases and in three of these there was evidence of progressive paralysis. This is in contrast to the group of arteriovenous fistulas in which only two of ten patients had associated impairment of function of peripheral nerves. Another contrast in the findings in these two groups of cases is that five of the false aneurysms and pulsating hematomas exhibited marked flexion deformities of the nearest joint while this complication occurred in only one of the ten arteriovenous fistulas. Close study of the pathology at the operating

table explains these differences. In the arteriovenous fistulas the tremendous force of the pressure of the circulating blood has an immediate outlet in the peripheral vascular bed of the venous system. Consequently, there is minimal fibrous reaction around such fistulas. However, in those patients in whom the artery is incompletely divided and there is no injury to a concomitant vein, the force of the blood pressure exerts itself in the direction of the tract of the missile. The musculature is damaged already by the missile. The subsequent clot formation, limited by the constricting confines of one or more adjacent fascial sheaths, sets up an inflammatory reaction which is reflected in a splinting of the part, the nearest joint being held in the position of flexion.

In the five patients in whom there was secondary swelling, the pulse rate varied from 80 to 90 beats per minute. Branham's sign was negative in the ten cases in this series. Compression of the swelling caused obliteration of the pulse distal to the lesion. Five of these patients complained of constant pain about the lesion and three were conscious of a buzzing or whirring sensation. In eight of the ten cases a systolic bruit was heard over the lesion.

For the reasons already indicated, operative therapy was instituted in all ten of the cases reported herein. Complete dissection of the false aneurysmal sac was possible in four cases. In five it was necessary to evacuate clot and then excise the torn segment of artery. In one case arterial plication was carried out successfully. Novocain block of the regional sympathetic ganglia was done postoperatively in six cases. Cure of the vascular lesions was effected in all patients and only two exhibited residual contracture at the time of release from this hospital. The average elapse of time between dates of injury and operation was thirty-eight days. One of the soldiers was returned to duty and nine were transferred to the United States for further physical therapy and rehabilitation.

SUMMARY

Report is made of experience with twenty cases of peripheral vascular lesions following war injuries. These cases constitute .49 per cent of 4,040 surgical battle casualties which were admitted to this general hospital from the campaigns on the Philippine Islands. There were ten cases of arteriovenous fistula, six cases of false aneurysm, and four cases of pulsating hematoma. It was a unique experience to observe several of these patients as the lesion developed from pulsating hematoma into false aneurysm. It was noted that the bruit over a pulsating hematoma is faint while that over a false aneurysm is relatively loud. The observation was made that the intensity of the bruit increases as the clot which forms soon after injury undergoes liquefaction. Hemorrhage from the wound was severe in only three of the patients with arteriovenous fistula and in only one with false aneurysm. Contracture of the joint nearest the vascular lesion was exhibited in only one of the arteriovenous fistulas, while five of those patients in whom there was incomplete arterial laceration developed regional flexion contracture soon after injury. This difference is explained by the findings at operation. The force of the arterial blood from an arteriovenous fistula is received in the peripheral venous system. In those patients in whom the artery is incompletely torn, the force of the arterial pressure expends itself

in the direction of the path of the missile. Subsequent clot formation in the region of damaged muscles is limited only by the confines of adjacent fascial sheaths. Inflammatory reaction is reflected in a splinting of the part, the nearest joint being held in flexion. Moreover, it has been observed that, at the time of secondary hemorrhage from a false aneurysm or a pulsating hematoma, there is severe pain and the angle of the flexion deformity increases while the bruit becomes less intense. Impairment of function of peripheral nerves was noted in only two of ten patients with arteriovenous fistula, while this complication was present in all ten of those with false aneurysm and pulsating hematoma. Primary emphasis in treatment was directed toward the healing of wounds and the development of collateral circulation. Operation was performed in this general hospital only in those patients in whom hemorrhage endangered life or the viability of an extremity, in those in whom contracture developed rapidly, or in those who showed progressive paralysis of peripheral nerves. Secondary external hemorrhage demanded immediate surgical intervention in one case. Secondary internal hemorrhage with the development of an hourglass type of pulsating hematoma developed in three cases of arteriovenous fistula, in two cases of false aneurysm, and in two cases of pulsating hematoma. Elapse of time between dates of injury and of secondary hemorrhage in these seven cases averaged thirty-four days. Photographs of specimens which are examples of pulsating hematoma secondary to rupture of aneurysm are shown. The secondary hematomas have developed in a fascial plane adjacent to that in which the primary aneurysm had formed. Experience with these patients has demonstrated that rest in bed and ordinary measures for immobilization of an extremity such as a sling or sandbags do not insure against the complication of secondary hemorrhage. Five of the twenty wounded soldiers whose records are reported herein were transported to the United States for definitive surgery.

None of the fifteen patients who were operated upon in this hospital showed signs of peripheral vascular insufficiency following operation. Elapse of time between dates of injury and operation averaged sixty-one days in the cases of arteriovenous fistula and thirty-eight days in the cases of false aneurysm and pulsating hematoma. In eight cases frequent block of the regional sympathetic ganglia with novocain was used as an adjunct to surgical excision of the lesion.

CAUSALGIA SECONDARY TO INJURY OF THE MAJOR PERIPHERAL NERVES

Treatment by Sympathectomy

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BURNING pain in the distal portion of an extremity following injury to a major peripheral nerve presented the same problem in World War II as it had in previous wars. Our experiences have indicated that this problem has not always been recognized, and on occasions there has been an unfortunate tendency to classify some of these patients as psychoneurotic. The pain closely follows the description given by Mitchell and associates in 1864 and designated by the term causalgia. A portion of their description of the signs and symptoms of causalgia is quoted because it is a classic in medical literature and little can be added today to this clear, complete, and concise portrayal of the clinical picture.

> The seat of burning pain is very various; but it never attacks the trunk, rarely the arm or thigh, and no oftener the forearm or leg. Its favorite site is the foot or hand. . . . . .
>
> The great mass of sufferers described this pain as superficial, but others said it was also in the joints and deep in the palm. If it lasted long, it was referred to the skin alone.
>
> Its intensity varies from the most trivial burning to a state of torture, which can hardly be credited but which reacts on the whole economy, until the general health is seriously affected.
>
> The part itself is not alone subject to an intense burning sensation but becomes exquisitely hyperesthetic so that a touch or a tap of the finger increases the pain. Exposure to the air is avoided by the patient with a care which seems absurd, and most of the bad cases keep the hand constantly wet, finding relief in the moisture rather than in the coolness of the application.
>
> As the pain increases, the general sympathy becomes more marked. The temper changes and grows irritable, the face becomes anxious and has a look of weariness and suffering. The sleep is restless and the constitutional condition reacting on the wounded limb exasperates the hyperesthetic state so that the rattling of a newspaper, a breath of air, another's step across the ward, the vibrations caused by a military band, or the shock of the feet in walking give rise to increase of pain. At last the patient grows hysterical, if we may use the only term which covers the facts. He walks carefully, carries the limb tenderly with the normal hand, is tremulous, nervous, and has all kinds of expedients for lessening his pain.
>
> The skin affected in these cases was deep red or mottled, or red and pale in patches. The epithelium appeared to have been partially lost, so that the cutis was exposed in places. The subcutaneous tissues were nearly always shrunken, and when the palm alone was attacked, the part so diseased seemed to be a little depressed

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> and firmer, and less elastic than common. In the fingers there were often cracks in the altered skin, and the integument presented of all the affected part was glassy, and shining as though it had been skillfully varnished.[1]

These are the fundamental symptoms and findings of the disease. Additional factors for accentuating the hyperesthetic state commonly found in modern life are the roar of an airplane, the whistle of a train or a boat, and gazing downward from a high building.

Present-day diagnostic aids only tend to confirm the clinical description as given by Mitchell. Investigations of the peripheral vascular mechanism of the involved extremity usually show changes. These have been found variable in the individual patient and even in the same patient as studied by the plethysmograph, the oscillometer, and modern skin temperature devices. The roentgenogram shows bone changes that may be related to the disease but which are more probably only those following disuse.

The exact etiologic mechanism of the production of pain seems to be little nearer solution today than at the time of Mitchell. There are various theories but they have such little support on basis of fact that there is no reason for their review.[2-7] Despite the lack of an adequate explanation for the etiology of the pain we feel that it has become established that interruption of the sympathetic nerve supply to the extremity greatly modifies or abolishes the symptoms of the disease.

It cannot be denied that the emotional status of the patient will activate the autonomic nervous system and may influence systemic reaction. This factor may assume too prominent consideration in the plan of treatment for causalgia. Although the clinical features of the disease should be well known, patients suffering from this disease continue to be admitted to hospitals with a diagnosis of severe psychoneurosis. Often transfer through several hospitals has been accomplished with a diagnosis of hysteria or severe psychoneurosis remaining as the primary diagnosis. A typical example of this can be cited in Case 1.

CASE REPORTS

CASE 1.—A 21-year-old private was admitted Jan. 24, 1945. The diagnosis was partial paralysis of the left sciatic nerve, cicatricial contracture of the left popliteal region, and severe psychoneurosis, mixed type, with hysterical, obsessive, and compulsive features.

He had been struck by shell fragments Aug. 8, 1944, which resulted in a severe lacerating wound of the left thigh. There was a profuse hemorrhage following the injury. He had the usual treatment for wounds of this type. When he regained consciousness he was aware of severe burning pain in the left foot, particularly in the plantar surface. There was complete motor paralysis of the left leg and foot. He complained bitterly of the persistent pain in the foot. Noises, jarring, vibrations, and touching dry objects with the hands caused paroxysms of pain. While using a washcloth on his hands he found some of the paroxysms of pain in the foot were diminished. He started holding a wet cloth in his hands continuously. He was evacuated from the combat area to the United States. Though there had been spontaneous return of function of the sciatic nerve, the pain was unimproved. Eighteen weeks after his injury he was seen by a psychiatrist because of the bizarre pain in the left foot and because he persisted in keeping the hands moist. The following opinion was given.

Dec. 15, 1944, this 21-year-old white private was referred for neuropsychiatric examination and appraisal because of nervous and hysterical type mannerisms (holding wash-

cloth in hands and wringing it continuously). He was relevant and coherent through the interview. He was thought to be of limited intelligence, and when questioned about holding the moist cloth he stated that he realized that it was a habit and not a desirable one. . . . . He stated that for some unknown reason this simple childish habit was of considerable comfort to him. He volunteered that he was gradually trying to hold the cloth less and less. . . . . His childhood history revealed that even at that time he resorted to fetishism. It is believed that a person with this patient's mentality might very easily regress to a childhood pattern at time of stress such as encountered by the patient since the wound. He was not examined from the neurologic standpoint because it was learned from his ward officer that he was to be transferred to a neurosurgic center for further treatment. Undoubtedly this man had a fixation requiring extensive and prolonged psychotherapy. It was not advisable at this time to attempt such therapy, and probably not until the left leg showed considerable improvement. Diagnosis was psychoneurosis, mixed type, hysterical, obsessive, and compulsive features, severe. He was then transferred to this neurosurgic center. Examination showed a partial paralysis of the left sciatic nerve and the typical findings of causalgia of the left foot.

On Jan. 29, 1945, twenty-six weeks after injury, a left lumbar sympathetic block was done with a transient complete relief of pain. On Jan. 31, 1945, a left lumbar sympathectomy was done with immediate complete relief of pain that has continued until the present. The washcloth was discarded immediately following the operation and no unusual behavior has existed after that time.

Prolonged delay in the treatment of the disease has been a usual occurrence. During this period of delay the changes of disuse affect the extremity. This is of particularly serious import when the hand is involved. Atrophy of soft tissues and periarticular fibrosis are prominent findings. Even after symptoms are relieved, prolonged treatment to regain the normal mobility of the part affected is necessary because of the organic changes from disuse. This, we believe, is primarily due to delay in treatment of the symptoms.

The treatment for the disease has largely been of three types: (1) treatment at the site of injury such as débridement and neurolysis, (2) complete division of the involved nerve, and (3) interruption of the sympathetic nerve supply to the affected extremity. In our group of patients we have been unable to find "trigger points" and have had no experience with elimination of the effects of such points.[3]

It has been the opinion of some who have seen the disease at an early stage that treatment at the site of injury is preventive or beneficial.[8] It has been recommended that a meticulous débridement be done, all devitalized tissue removed, and the nerve repaired if grossly injured. If the accompanying artery has been irreparably damaged, the destroyed area should be excised. We have not seen patients with causalgia until several weeks following injury and can give no evaluation of local treatment at an early stage of the disease. However, we have been impressed with the small benefit derived from local procedures in the late phases of the disease. In fact, some patients have shown an exacerbation of symptoms following local operative procedures. A typical example of this is cited in Case 2.

CASE 2.—A 29-year-old white man was admitted Feb. 13, 1945, transferred from another hospital. He had been struck in the left axilla by a rifle bullet Dec. 8, 1944. There was a simple penetrating wound with complete motor and sensory paralysis of the left arm,

forearm, and hand. Immediately after the injury he had severe burning pain in the left hand. The pain prevented all rest, and he lost 15 per cent of his weight. He was given some medication for pain which made it bearable. After about four weeks' time there was spontaneous subsidence but not complete disappearance of pain. On admission to this hospital the pain was no longer troublesome.

Neurologic examination showed complete paralysis of the ulnar, median, radial, and musculocutaneous nerves. The blood count, urine, and blood serology were within normal limits.

Twelve weeks after his injury an exploration of the nerves of the arm was done. The ulnar, radial, and musculocutaneous nerves were found to be completely divided and were repaired by end-to-end sutures. The lateral half of the median nerve was also found to be divided but the medial half of the nerve was only dissected from the surrounding scar tissue.

Immediately following the operation the severe burning pain in the palmar surface of the hand recurred. After ten days a procaine block of the sympathetic supply to the upper extremity was done. He had a complete relief of pain that lasted thirty-six hours; the pain then returned though in lesser severity. The patient preferred to await spontaneous resolution of pains rather than to have a dorsal sympathectomy. Four weeks after operation all pain had ceased.

When exploring the involved nerve in patients with causalgia, it is rare to find the nerve completely divided. Usually there is a neuromatous area at the site of injury and occasionally no grossly abnormal area can be found. In only two patients of this group was the nerve found to be completely divided. Others have observed that true causalgia can occur in the distribution of a nerve that has been completely divided.[2, 8] Often the muscles supplied by the involved nerve show excellent contractile function though voluntary movement is grossly limited because of pain. Under such circumstances one is loathe to section the nerve in order to obtain relief of pain. If, at exploration, the nerve has suffered such extensive damage that it is doubtful that effective function will be regained spontaneously, excision of the damaged segment and suture of the nerve will frequently provide relief from pain.

The interruption of the sympathetic nerve supply to the involved extremity has proved to be the most useful procedure for the relief of causalgia in this series of patients. Periarterial sympathectomy was formerly used extensively in attempting to interrupt completely the sympathetic supply to an extremity.[2] It has become definitely established that this method is only partially successful. Direct attack on the ganglia supplying the extremity has largely supplanted the arterial stripping methods. The two may be used in conjunction, although we have not found it necessary to do so.

Temporary interruption of the sympathetic supply by procaine block of the sympathetic ganglia to the involved extremity is first done.[9, 10] If relief is obtained for one-half to one hour, excision of the sympathetic supply to the extremity will also be effective. Two patients of this series have obtained permanent relief from a single procaine block but it has been our experience that repeated chemical blocks usually have not produced permanent relief. Surgical excision has been preferred to alcohol block. After experiencing the relief obtained, the patient is permitted to decide if he desires the operative procedure.

The usual methods of sympathectomy have been employed. A muscle-splitting extraperitoneal approach for removal of the second and third lumbar ganglia has been used for producing preganglionic sympathectomization of the lower extremity.[11] Recently a modification of the thoracolumbar operation described by Smithwick[12] for use in hypertension has been employed for a more complete sympathectomization of the thigh. The Smithwick procedure has been used for sympathectomization of the upper extremity.[13, 14] It has the advantage of being a preganglionic excision, of producing permanent results, and eliminating the Horner's syndrome incurred by some methods. It has been felt that it was not justified to incur a Horner's syndrome with permanent disfigurement when the dorsal approach has proved completely adequate. There have been no serious postoperative complications.

Although the paroxysmal, peripheral burning pain is relieved by these methods, there is often a residual discomfort that is experienced by practically all peripheral nerve injuries. When pain is relieved, voluntary movement is re-established and the necessary treatment can be given to return the extremity to a state of normal function.

During the past twelve months, sixty-seven patients have been admitted to this hospital with injury to a major peripheral nerve and causalgia of sufficient severity to warrant some form of treatment. The lower extremity has been involved in forty-four, the upper extremitiy in twenty-three patients. The seat of the maximum pain has been in the distribution of the posterior tibial nerve or the median nerve in all instances. This is not in agreement with other reported series.[2, 15] Usually the entire extremity has been designated as affected until more careful questioning and evaluation has established pain of greatest severity to the peripheral distribution of a specific nerve. The time of onset of pain has varied. It may be concomitant with the injury or occur several weeks following the injury. The posterior tibial has often been involved at the time of operative procedures for intractable hemorrhage from the tibial vessels. Concomitant injury of the accompanying blood vessels has been apparent in many instances of the present series although in all probability many of the others had vascular injury that were not recognized due to an incomplete lesion and the excellent collateral circulation present in the patients of this age group.

Sympathectomization of the involved extremity has been done in thirty patients; in twenty-two for lower extremity and in eight for upper extremity involvement. Two additional patients have had only the area of injury sympathectomized and are not included in this report.

It has been necessary to reoperate on one patient to obtain a more complete sympathectomization of the lower extremity. In one instance removal of the first and second lumbar ganglia was done after removal of the third and fourth ganglia had been ineffective (Table I, Case III). Complete relief of pain in the affected extremity was obtained by the more extensive operation. It is now our relief that the operation should always be of sufficient extent to sympathectomize the area of the site of nerve injury as well as the area of maximum pain.

TABLE I. CAUSALGIA OF LOWER EXTREMITY

CASE NO.	DATE OF INJURY	SITE OF INJURY	PRELIMINARY TREATMENT	DATE & EXTENT OF SYMPATHECTOMY	RESULT
I	June 21-44	Buttocks	Neurolysis, lumbar block	Aug. 8-44 L-2, L-3	Failure
II	June 12-44	Thigh, proximal third	Lumbar block	Aug. 12-44 L-2, L-3	Excellent
III	July 18-44	Popliteal space	Neurolysis, lumbar block	Sept. 4-44 L-2, L-3	Good
IV	June 23-44	Thigh, middle third	Lumbar block	Sept. 4-44 L-3, L-4	Failure
				Mar. 19-45 L-1, L-2	Excellent
V	Aug. 17-44	Thigh, middle third	Lumbar block	Nov. 20-44 L-2, L-3	Good
VI	July 14-44	Leg, middle third	Lumbar block	Nov. 29-44 L-2, L-3	Excellent
VII	May 23-44	Thigh, middle third	Lumbar block	Jan. 11-45 L-1, L-2, L-3	Excellent
VIII	July 4-44	Leg, proximal third	Lumbar block	Jan. 15-45 L-2, L-3	Good
IX	Oct. 31-43	Leg, middle third	Lumbar block	Jan. 24-45 L-2, L-3	Good
X	July 20-44	Thigh, proximal third	Lumbar block	Jan. 24-45 L-1, L-2, L-3	Good
XI	July 19-44	Leg, middle third	Neurolysis, lumbar block	Jan. 29-45 L-2, L-3	Excellent
XII	July 6-44	Thigh, proximal third	Lumbar block	Jan. 31-45 L-2, L-3	Good
XIII	Aug. 8-44	Thigh, distal third	Lumbar block	Jan. 31-45 L-1, L-2, L-3	Excellent
XIV	June 10-44	Thigh, middle third	Lumbar block	Feb. 5-45 L-2, L-3	Good
XV	July 13-44	Buttocks	Lumbar block	Feb. 5-45 L-2, L-3	Good
XVI	Aug. 20-44	Thigh, proximal third	Lumbar block	Feb. 8-45 L-2, L-3	Good
XVII	July 27-44	Thigh, middle third	Neurolysis, lumbar block	Mar. 2-45 L-2, L-3	Good
XVIII	Sept. 29-44	Leg, middle third	Lumbar block	April 13-45 L-2, L-3	Good
XIX	Dec. 21-44	Thigh, distal third	Lumbar block	May 14-45 L-2, L-3	Good
XX	Jan. 11-45	Thigh, distal third	Lumbar block	May 24-45 L-2, L-3	Good
XXI	Mar. 4-45	Thigh, distal third	Lumbar block	June 4-45 L-2, L-3	Good
XXII	Dec. 15-44	Thigh, distal third	Lumbar block	June 20-45 L-2, L-3	Good

Results were judged by the relief of pain experienced and the ability to use the affected extremity. Results were good to excellent in twenty-eight patients (Tables I and II). Two patients of this series did not obtain relief by sympathectomy. Before the more complete operation was resorted to, a cordotomy was done in one patient, after removal of the second and third lumbar ganglia had failed to give relief of pain (Case I, Table I); the nerve injury was in the proximal third of the thigh and the site of injury had not been sympathectomized. The second failure had a completely technically satisfactory dorsal sympathectomy yet there was no relief of symptoms; we have no adequate explanation for the failure in this instance.

TABLE II. CAUSALGIA OF UPPER EXTREMITY

CASE NO.	DATE OF INJURY	SITE OF INJURY	PRELIMINARY TREATMENT	DATE & EXTENT OF SYMPATHECTOMY	RESULT
I	Aug. 8-44	Arm, proximal third	Neurolysis, dorsal block	Jan. 24-45 D-2, D-3	Excellent
II	Nov. 13-44	Arm, proximal third	Neurolysis, dorsal block	Feb. 16-45 D-2, D-3	Excellent
III	Dec. 15-44	Forearm, middle third	Dorsal block	Feb. 19-45 D-2, D-3	Excellent
IV	Nov. 26-44	Forearm, distal third	Dorsal block	April 9-45 D-2, D-3	Good
V	Nov. 6-44	Clavicular region	Neurolysis, dorsal block	April 13-45 D-2, D-3	Failure
VI	Feb. 8-44	Clavicular region	Dorsal block	June 5-45 D-2, D-3	Good
VII	Mar. 9-44	Axilla	Dorsal block	June 11-45 D-2, D-3	Excellent
VIII	Dec. 20-44	Arm, middle third	Neurolysis	June 20-45 D-2, D-3	Excellent

Not included in this group of patients with causalgia following major peripheral nerve injuries were three patients with burning pain in the lower extremity following cauda equina injuries. Lumbar sympathectomies have been done on these patients without benefit. The site of injury was not sympathectomized and may well have some bearing on the failure.

SUMMARY

1. Causalgia concomitant with injuries of the major peripheral nerves presented a real problem of management in World War II, as in preceding wars.

2. During the past year there have been sixty-seven patients with major peripheral nerve injuries and concomitant causalgia of sufficient severity to require treatment admitted to this hospital.

3. Thirty of this group desired sympathectomy after experiencing the relief obtained by sympathetic block.

4. Of this group twenty-two had lumbar sympathectomies and eight had preganglionic dorsal sympathectomies.

5. Good to excellent results were obtained in twenty-eight of the patients. Failure to relieve symptoms and re-establish use of the affected part occurred in two patients.

6. The sympathectomization should be of sufficient extent to include the area of injury as well as the area of symptoms.

7. Early sympathectomization of the affected extremity including the area of injury will, in the vast majority, relieve the symptoms of the disease and prevent the profound disabilities of disuse.

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GUNSHOT WOUNDS OF THE ABDOMEN

A Review of 149 Cases

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IN THIS paper is given an analysis of 149 gunshot wounds of the abdomen and gunshot wounds of the abdominal wall treated at Harlem Hospital over an eleven-year period, from 1933 to 1944. Thirty-five of these cases were included in a report by McGowan[1] in 1935. The high mortality of these injuries caused us to make this study and the relative paucity of reports on this subject made it seem worth while to record our experiences and what we have learned about the emergency handling of these cases. Most of the principles that we follow even at the present time were outlined by Connors[2] from this hospital in 1923 and amplified by the subsequent reports of Silleck,[3] Eisberg,[4] and McGowan.[1] Their papers were reports of penetrating wounds of the abdomen in which gunshot wounds were combined with stab wounds. It is now generally agreed that because of the more serious character of gunshot wounds they should be studied separately.

Our survey includes 115 penetrating gunshot wounds of the abdomen and 34 gunshot wounds of the abdominal wall. The patients in this series were operated upon by the surgeon who happened to be on duty at the time of the patient's admission.

FREQUENCY

Gunshot wounds in general are not as frequent in New York City as they are in some of our southern cities due to the fact that it is against the New York law to carry or have a pistol without a permit. Therefore, this series of cases is not as large as others that have been reported for the same period of time from cities where there is no such law.

All wounds in this series were inflicted by pistol bullets; we have had no experience with shotgun injuries.

It should also be pointed out that injuries of this character in civil life carry, as a rule, a higher mortality than that obtained in military life, because the average soldier is a more rugged physical specimen and reacts better physiologically, when injured, than the average large city civilian. It has been our experience, with the few soldiers whom we have treated, suffering from any type of trauma, that they have much greater powers of recuperation than other citizens.

DIAGNOSIS

The diagnosis of gunshot wound or wounds of the abdomen is usually as simple as the injury is obvious. The chief point of interest to the surgeon

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is whether or not there has been an intra-abdominal injury, and the decision for or against operation depends upon this. This decision is, at times, difficult to make. When there is the slightest doubt as to whether a blood vessel or a viscus within the abdomen is injured, the patient should be subjected to immediate exploratory laparotomy. Connors insisted upon careful inspection of the bullet wound and its direction and a decision as to whether it was one of entry or exit. If there are several wounds, it is important to know how many of these are of entry and how many of exit. The location of the incision is, in part, governed by this and is helpful in making a tentative diagnosis of visceral injury. The path of the bullet should be mentally visualized, if possible, by the surgeon at the time of operation. Palpation will indicate rigidity, tenderness, and rebound tenderness, which are signs of peritoneal irritation, and in cases where there is doubt as to whether or not the peritoneal cavity has been entered, they are of great diagnostic value. Oberhelman and Le Count[5] have pointed out that side-to-side injuries in the abdomen are the most serious; bullets entering from front to back are the next most serious; and those entering from the back are usually the least serious.

In Table I, it is of interest to note that 64.3 per cent of the patients with penetrating gunshot wounds of the abdominal wall had tenderness, 66.1 per cent had abdominal rigidity, while none of those with nonpenetrating wounds showed abdominal rigidity, only 11.7 per cent showed tenderness, and none showed vomiting.

TABLE I

TYPE OF GUNSHOT WOUND	NUMBER OF CASES	TENDERNESS		ABDOMINAL RIGIDITY		VOMITING	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Penetrating	115	74	64.3	76	66.1	5	4.3
Nonpenetrating	34	4	11.7	0	0	0	0

The percentage of cases with abdominal tenderness and abdominal spasm is lowered by the fact that seventeen patients were unconscious at the time of admission to the hospital, in profound shock, and with obvious penetrating gunshot wounds of the abdomen. Our percentage of patients with vomiting in penetrating gunshot wounds of the abdomen is only 4.3 per cent (five cases), whereas Hamilton and Duncan[6] reported vomiting in 46 per cent of their patients, while Storck[7] reported only three cases of nausea and vomiting in a series of forty-six cases.

The amount of abdominal tenderness and spasm is found to be in direct proportion to the amount of blood in the peritoneal cavity or to the amount of spillage from the gastrointestinal tract.

The passage of fresh blood by rectum, urethra, or mouth points to the injury of the lower bowel, urinary tract, or stomach, and immediate exploration is indicated in these cases regardless of other abdominal findings. In this series there were found the following figures: bleeding per rectum, 1 case; bleeding per urethra, 9 cases; and hematemesis, 2 cases.

RADIOGRAPHIC FINDINGS

Roentgenologic study has helped us in these cases. Where there is no wound of exit of the bullet, a roentgenogram taken immediately with a portable x-ray machine at the time of admission will help locate the bullet and aid the surgeon in visualizing in his mind the path the bullet has taken; in some instances, if the patient is not in serious condition, free gas under the diaphragm, seen in the x-ray view of a patient sitting upright, is evidence of a perforation of the gastrointestinal tract. Occasionally this is the sole proof of perforation of a hollow viscus.

In Table II it is seen that the presence of gas under the diaphragm on x-ray examination is practically pathognomonic of intestinal tract perforation.

TABLE II. RADIOGRAPHIC FINDINGS IN TWENTY-TWO CASES

	NUMBER OF CASES	OPERATION
Pneumoperitoneum	15	Gastrointestinal tract perforation
Pneumoperitoneum absent	6	No perforation
Pneumoperitoneum absent	1	Two small perforations of the gastrointestinal tract

ABDOMINAL TAP

In difficult cases, as a diagnostic aid, we have also used abdominal tap. Peritoneal tap, using a spinal puncture needle, is performed in all four abdominal quadrants. In this series of cases, eight abdominal taps were performed; in five cases, the tap was positive with blood being obtained. At operation in these five cases, free blood was found in the peritoneal cavity. In three cases the abdominal tap was negative and no free fluid or perforation of the intestinal tract was found. A negative abdominal tap does not mean that there can be no intra-abdominal injury, but it is reasonably certain that a massive intra-abdominal hemorrhage will be diagnosed by peritoneal tap if the abdominal puncture is properly performed. Dixon, Martin, and Ochsner[8] have recently recommended abdominal tap as helpful.

In Table III are listed the reports of the authors having the largest series of cases, with their operative findings, together with our own.

The age incidence is indicated in Table IV; this reveals that the mortality is definitely higher after the age of 31 years. Hamilton and Duncan also observed that the mortality rate is higher in gunshot wounds of the abdomen

TABLE III

AUTHOR	NUMBER OF CASES	OPERATIVE MORTALITY (PER CENT)
Oberhelman and Le Count	301	61.4
Rippy	292	61.9
Hamilton and Duncan	182	48.9
Taylor	101	60.0
Elkin and Ward (pistol and rifle wounds)	176	47.7
Wilkinson, Wright, and Hill	115	60.0

In Elkin and Ward's series of 176 penetrating wounds, there were seven cases in which no perforations were found.

TABLE IV. AGE INCIDENCE

DECADE	PENETRATING	NONPENETRATING	DEATHS	MORTALITY (PER CENT)
1-10	0	0	0	0.0
11-20	16	4	6	30.0
21-30	56	15	32	45.0
31-40	27	7	19	55.8
41-50	9	7	8	50.0
51-60	3	1	3	75.0
61-70	1	0	1	100.0
Unknown	3	0	3	100.0

in the older age groups. Rippy's[9] series is also in agreement with this finding and he suggests that one of the reasons for the greater vulnerability of the older patients is that arteriosclerosis prevents effective vasoconstriction.

By far the greatest cause of death in gunshot wounds of the abdomen is hemorrhage and the resulting shock. In Table V is recorded the presence or absence of shock in 115 patients with penetrating wounds of the abdomen. It is seen that in this series 77.03 per cent of the patients that were admitted to the hospital in shock died, whereas only 36.6 per cent of the patients admitted who were not in shock died.

TABLE V. PRESENCE AND ABSENCE OF SHOCK ON ADMISSION

CONDITION ON ADMISSION	NUMBER OF CASES	LIVED	DIED	MORTALITY (PER CENT)
In shock	74	17	57	77.03
Not in shock	41	26	15	36.6

The mortality for this series is shown in Table VI. The mortality of thirty-four gunshot wounds of the abdominal wall, even without operation, was 0. It is to be noted that there were eleven patients who died before operation, and the mortality was 100 per cent. We have included in this series of cases every patient that reached the hospital alive. We did not attempt to sort out moribund cases from others because we felt a truer picture of the situation could be obtained in this way. The mortality of 104 operative cases was 60 per cent. The important preoperative point in regard to therapy in these cases is to stop hemorrhage and to counteract shock by means of transfusion, plasma, and intravenous fluids. The critical period in the treatment of these patients is the first twenty-four hours. Thirty-two of the sixty-one operative deaths occurred during the first twenty-four hours after operation; thus, a little over one-half, or 52.4 per cent, of all operative deaths

TABLE VI. SUMMARY OF 149 CASES OF GUNSHOT WOUNDS OF THE ABDOMEN AND ABDOMINAL WALL

TYPE OF GUNSHOT WOUND	NUMBER OF CASES	DIED	LIVED	MORTALITY (PER CENT)
Penetrating of abdomen	115	72	43	62.6
Operative cases of abdomen	104	61	43	60.0
Of abdominal wall with no operations	34	0	34	0.0
Penetrating of abdomen, patient died before operation	11	11	0	100.0

occurred within the first twenty-four hours. In thirty-four cases the systolic pressure on admission was 170 mm. of Hg and in forty cases the blood pressure, systolic, was 70 mm. of Hg or lower. All patients should receive antitetanic serum and antigas gangrene antitoxin upon admission. Most delay before transfusion is caused by the time it takes to determine the patient's blood type.

ANESTHESIA

We used open cone ether in all of our cases and found it to be the most satisfactory type of anesthesia. Spinal anesthesia is to be condemned because it increases shock and increases spill of intestinal content. The type of incision used depends upon the point of entrance and the probable path of the bullet. Too much emphasis cannot be placed upon the greatest speed possible in operating compatible with good, careful surgery. Connors, Eisberg, and McGowan have pointed out the need for incisions of adequate length and evisceration if there is difficulty in exposing the lesion. The method of examination advocated by Elkin and Ward[10] is excellent, that is, the cecum is examined first; the small intestine is then inspected throughout its length up to the ligament of Treitz, and any perforations are closed when found; the large intestine is explored next; then the stomach and retroperitoneal structures are examined. Each surgeon usually explores the abdomen according to his own method.

Table VII shows that the frequency of injury is, in the main, in proportion to the space occupied by the viscus within the peritoneal cavity.

TABLE VII. INJURIES TO ABDOMINAL VISCERA

Small intestine	47
Large intestine	37
Stomach	30
Liver	27
Diaphragm	12
Mesentery	10
Omentum	8
Urinary bladder	6
Kidney	5
Spleen	6
Gall bladder	3
Pancreas	1

TABLE VIII. ASSOCIATED INJURIES—BULLET WOUNDS

Extremities		32
Lower	20	
Upper	12	
Chest, penetrating		14
Head		4
Neck		2
Buttock		2
Mandible		1
Penis		1
Scrotum		1
Fractured rib with chest		1
Spine with chest		1
Total		59

This group of cases had an exceptionally large number of associated injuries; in fact, 59 of the 149 cases had associated extra-abdominal injuries. This, of course, has a very direct bearing on mortality and plan of treatment.

In Table IX is shown the mortality in relation to associated injuries.

TABLE IX. MORTALITY WITH AND WITHOUT ASSOCIATED INJURIES

PERFORATION OR LACERATION OF	LIVED	DIED	MORTALITY (PER CENT)
Small intestine	7	7	50.0
Small intestine with associated injuries	8	25	75.7
Stomach	3	4	57.1
Stomach with associated injuries	4	19	82.6
Liver	5	2	28.5
Liver with associated injuries	6	14	70.0
Large intestine	3	5	62.5
Large intestine with associated injuries	6	23	79.3
Diaphragm	0	0	0.0
Diaphragm with associated injuries	2	10	83.3
Urinary bladder	3	0	0.0
Urinary bladder with associated injuries	0	3	100.0
Kidney	2	0	0.0
Kidney with associated injuries	1	2	66.6
Spleen	1	0	0.0
Spleen with associated injuries	2	3	60.0

The mortality rate for perforation of any single viscus is highest in perforation of the large bowel. In this series, as is shown in Table IX, there were eight perforations of the large intestine alone and there were five deaths, which gives a mortality of 62.5 per cent. There were a total number of twenty-nine cases of perforation of the large bowel with associated injuries and in this group the mortality rate was 79.3 per cent. It should also be pointed out that it is relatively unusual to have a perforation solely of the large bowel, because when there is large bowel injury usually some associated lesion exists. The high mortality rate in perforation of the large intestine is due to the higher bacterial count found at this level of the intestine and the spillage into the peritoneal cavity in most cases leads to a peritonitis which is often fatal. In the transverse colon and in the sigmoid, exteriorization of the intestine, in our opinion, is of value. Hamilton and Duncan observed that there was a progressive increase in mortality from peritonitis as the level of the perforated bowel descends from jejunum to colon. However, Storck reported in his series of cases a relatively low mortality in colonic injuries and stated that it was due probably to the relatively small quantity of spillage which ordinarily accompanies such injuries. It has been our experience that sulfonamides placed in the peritoneal cavity at the time of operation, and followed by sulfonamides by mouth or intravenously, have not reduced the mortality rate in these cases. This is contrary to the published reports of others. We use sulfonamides routinely and will continue to do so, but it just happens that our results to date with their use have not been as impressive as the results reported by other clinics.

Perforations of the stomach show a mortality rate of 57.1 per cent, while perforations of the stomach plus associated injuries give a mortality rate of

82.6 per cent. Rippy found his mortality rate for stomach injuries alone to be 53.3 per cent and in his cases where the stomach injury was associated with another lesion the mortality rate was 65.2 per cent. Hamilton and Duncan pointed out that perforation of the stomach and duodenum gives a rather high mortality rate because of the relatively large associated blood loss, the difficulty of exposure, and often the frequency of associated thoracic injury. Our study is in agreement with these quoted authors and we also found that there was a higher incidence of postoperative pneumonia in patients with stomach perforation than in any other group. Perforation of the small intestine had the lowest mortality rate of any segment of the gastrointestinal tract, which was 50 per cent for perforation of the small bowel alone and 75.7 per cent where there were associated injuries.

The mortality rate in patients with chest and coincidental abdominal injuries was 83.3 per cent. This is in striking contrast to those admitted to the hospital with a perforated injury of the chest alone, as the majority of these patients recovered on a conservative regime. Hardt and Seed[11] reported a mortality of 56 per cent. Injuries to the liver gave a mortality rate of 28.5 per cent and injuries of the liver plus associated injuries gave a mortality rate of 70 per cent. We had twenty-seven cases of liver injuries with sixteen deaths and three of the patients exhibited the symptoms that go with the so-called "liver death." The syndrome of "liver death," as described by Heyd,[12] is characterized by high temperature, falling blood pressure, circulatory collapse, coma, and then death. The blood loss in these three cases was insufficient to produce the symptoms that we found.

It was pointed out by Oberhelman and LeCount that the number of perforations of a hollow viscus has a direct bearing on mortality. This is confirmed by us, as shown in Table X. Of the 104 patients operated on, 43 lived, 61 died, and 12 of these 61 had associated injuries of head, neck, chest, or extremities.

TABLE X. DIFFERENTIAL MORTALITY IN RELATION TO NUMBER OF PERFORATIONS OF GASTROINTESTINAL TRACT

NUMBER OF PERFORATIONS OF GASTROINTESTINAL TRACT	DIED	LIVED	MORTALITY (PER CENT)
1	12	11	52.2
2	18	11	62.1
3	10	3	76.9
4	2	4	33.3
5	2	0	100.0
6	2	0	100.0
7	2	0	100.0
8	5	1	83.3
9	1	1	50.0
11	1	1	50.0
12	1	1	50.0
13	1	0	100.0
15	1	0	100.0
16	1	0	100.0
Total	59	33	

POSTOPERATIVE COMPLICATIONS

Hemorrhage and shock are the most common postoperative complications. Following operation, after hemorrhage has been controlled, postoperative shock is superimposed upon the shock and hemorrhage due to the original injury. In the 115 penetrating wounds, 74 patients entered in shock; 57 died, which gave a mortality rate of 77.03 per cent, as shown in Table V. We noted that 52.4 per cent of all operative deaths occurred within the first twenty-four hours, which indicates the seriousness of shock as a death-producing factor. The other postoperative complications noted in this series are tabulated in Table XI. Twenty patients in this series developed peritonitis and died.

TABLE XI. POSTOPERATIVE COMPLICATIONS

COMPLICATION	NUMBER OF CASES	LIVED	DIED	MORTALITY (PER CENT)
Clinical peritonitis	20	0	20	100.0
Pneumonia	12	7	5	41.7
Evisceration	2	2	0	0.0
Subphrenic abscess	1	0	1	100.0
Infected retroperitoneal hematoma	1	1	0	0.0
Intestinal obstruction due to adhesions	1	0	1	100.0

Twelve patients developed clinical postoperative pneumonia and eight of these were patients that had combined chest and abdominal injuries and, as shown in Table XI, seven recovered. Evisceration occurred in two patients. In one it occurred on the fourteenth day after operation and in the other, who developed pneumonia on the fourth day postoperatively, on the seventh; both were preceded by a serosanguineous discharge from the wound. In this series the percentage of evisceration was 2.9 per cent, as compared with 5.6 per cent obtained by Hamilton and Duncan and 3 per cent, as observed by Taylor.[13] This is slightly higher than the occurrence of evisceration for laparotomies in general, which is placed usually between 0.5 per cent and 1 per cent. One patient developed a subphrenic abscess following perforation of the small intestine (eight perforations) on the ninth postoperative day and this patient died on the sixth day after drainage of the subphrenic abscess. In one case a retroperitoneal hematoma became infected twenty-four days after operation. This was incised and a large abscess cavity was found which contained about 800 c.c. of thin, yellowish pus with a foul odor; the cavity extended upward almost to the costal margin in the posterior axillary line and downward almost to the internal abdominal ring and posteriorly to the border of the rectus spinus muscles. The patient made an uneventful recovery and was discharged on the sixteenth postoperative day. One patient developed postoperative adhesions with resultant intestinal obstruction and was operated upon on the thirty-third day following the first operation (there were two perforations of the jejunum about six inches below the ligament of Treitz). In the second operation there were numerous fine and moderately firm adhesions matting the intestines together on the left side of the abdomen. This patient died on the sixth day following operation.

POST-MORTEM FINDINGS

Excepting for the splendid detailed report of Oberhelman and Le Count, too few of the recent excellent articles on this subject from the larger clinics have given in detail the post-mortem findings in the fatal cases. This we consider very important.

Post-mortem examinations were made on all of the patients who died in this series by the medical examiners of New York City, and the following reports were made available to us for study.*

In Table XII, the cause of death, as determined by autopsy, is listed and is self-explanatory.

TABLE XII. CAUSE OF DEATH IN SEVENTY-TWO CASES BY POST-MORTEM EXAMINATION

CAUSE OF DEATH	NUMBER OF CASES
Hemorrhage and shock	32
Peritonitis	29
Pneumonia	5
Retroperitoneal phlegmon	4
Embolus to lung	1
Septic pleuritis	1

PATIENTS WHO DIED BEFORE OPERATION COULD BE STARTED

It is of interest to note that in eight of the eleven cases in which the patient died before operation could be started the cause of death was hemorrhage and shock due to a bullet wound of a large blood vessel, as shown in Table XIII. In two cases the patients died from shock and hemorrhage due to gunshot wound of the liver, in five hemothorax and hemoperitoneum. This only emphasizes

TABLE XIII. AUTOPSY FINDINGS IN ELEVEN PATIENTS WHO DIED BEFORE OPERATION

CASE NO.	TIME ELAPSING BEFORE DEATH	AUTOPSY FINDINGS
1	4 hr.	Hemothorax and hemoperitoneum; bullet wound of liver 1000 c.c. of blood in right pleural cavity and 300 c.c. in the peritoneal cavity
2	30 min.	Bullet wound of lower lobe of right lung, inferior vena cava, external iliac vein; hemoperitoneum
3	1 hr.	Bullet wound of right iliac artery and vein; 8 perforations of small intestine
4	1 hr.	Laceration of vena cava, hemoperitoneum; 500 c.c. of blood in right chest
5	45 min.	Perforation of liver, right diaphragm, and anterior and posterior walls of stomach; 500 c.c. of blood in peritoneal cavity and 1,300 c.c. of blood in right pleural cavity
6	30 min.	Perforation of right common iliac vein and artery, perforation of the jejunum 8 inches from the ligament of Treitz and 2 perforations of the ileum
7	30 min.	Laceration of abdominal aorta, hepatic artery and vein, left renal vein, and left kidney
8	1 hr.	Laceration of left saphenous vein, hemoperitoneum; 12 perforations of the jejunum
9	2 hr.	Hemoperitoneum; 10 through-and-through perforations of the jejunum
10	15 min.	Complete severance of abdominal aorta, inferior vena cava; duodenum completely severed, perforation of the liver
11	15 min.	Bullet wound of left external iliac artery and vein, through-and-through perforation of the rectum, 12 perforations of the small intestine

*Through the courtesy of Dr. Thomas A. Gonzales, Chief Medical Examiner.

the fact that the greater the degree of shock the greater the indication for immediate operation so that hemorrhage can be controlled.

LESIONS MISSED AT OPERATION

The group of cases in which the lesions of importance were missed by the surgeon during the operation is outlined in Table XIV.

TABLE XIV. LESIONS OVERLOOKED AT OPERATION

CASE NO.	POSTOPERATIVE DAY OF DEATH	MISSED LESION FOUND AT AUTOPSY	CAUSE OF DEATH
1	9th	Perforation through-and-through of the lower portion of the rectum; patient developed a perirectal phlegmon	Peritonitis
2	4th	Perforation of the ascending colon 10 inches above the ileocecal junction measuring ⅝ and ¼ inches in diameter	Peritonitis
3	6th	Perforation of the pericardium	Pericarditis
4	2nd	Two perforations in the descending colon near the splenic flexure	Peritonitis
5	9th	Perforation of the duodenum near its pancreatic border about ½ inch in length, and a through-and-through perforation of the stomach 3 inches from the pylorus	Peritonitis
6	1st	Two perforations of the distal portion of the duodenum and the anterior wall	Hemorrhage and shock
7	1st	Laceration of the lower pole and the middle part of the spleen	Hemorrhage and shock
8	2nd	Small perforation ¼ inch in diameter of the aorta at the level of the 11th dorsal vertebra	Hemorrhage and shock
9	1st	Perforation of the left iliac artery	Hemorrhage and shock
10	1st	Two lacerations of the left iliac vein	Hemorrhage and shock

Five perforations of the gastrointestinal tract were not sutured at the time of operation. There were three lacerations of the major blood vessels that were missed by the surgeon. There was one laceration of the spleen that was not found and one of the pericardium. Of the missed perforations of the gastrointestinal tract, two were of the duodenum, one of the ascending portion of the colon, one of the descending colon, and one of the rectum. From Tables XIII and XIV it is to be noted that injuries to major blood vessels are not uncommon and are a cause of very rapid death.

In this series there were, therefore, ten cases in the seventy-two deaths where a fatal injury was missed at the time of operation, or in 13.8 per cent of the cases. It is important to realize that speed must not be at the expense of care, and, too, that every surgeon in the handling of these cases should develop a plan of investigation at the time of operation that will not permit of the possibility of overlooking a serious injury except under bizarre circumstances. The exploration should be done with great care, speed, and thoroughness. It has been our feeling that most missed lesions were the result of incisions that were too short and did not permit of sufficient visualization.

COMBINED THORACIC AND ABDOMINAL INJURIES

In thoraco-abdominal injuries the bullet wound of entrance is, in the majority of instances, in the chest. In only one case out of fourteen was there a

lesion found within the chest where the wound of entrance was solely to be found in the abdominal wall. In nine cases out of the fourteen, the bullet wound of entrance was in the chest and penetrated to the abdomen. This is explained by the fact that the patient was in a bending or stooped position at the time of injury. It is therefore wise for surgeons when investigating chest injuries to keep in mind the possibility of a concomitant intra-abdominal lesion.

In Table XV there are listed the data on twelve fatal cases of thoraco-abdominal wounds.

In this series there were three fatal cases of combined abdominal and head injuries. In one case the patient was unconscious on admission and presented a bullet wound of entrance in the left upper quadrant one inch below the costal margin and a bullet wound of the left temporal region of the skull; he died one hour after admission to the hospital. In another case the patient showed bullet wounds in the anterior portion of the temporal region, but x-ray of the skull was negative for fracture, and one wound of the right lower quadrant. At operation four perforations of the ileum and one of the cecum were found. This patient died on the sixth postoperative day. The third patient showed a gunshot wound of the right temporal region and of the chest, the third intercostal space in the right midclavicular line, and at operation he showed a perforation of the diaphragm and dome of the liver and died on the first postoperative day.

TREATMENT

Penetrating abdominal wounds should be explored promptly, but opinion is divided as to the advisability of delaying operation to treat shock. The routine at Harlem Hospital is to determine the patient's blood type at once and to start intravenous infusion of normal saline solution immediately, continuing it until blood is available and then substituting blood for the normal saline solution. Storck and Rippy advise against operating, if possible, until the patient's blood pressure has risen above a critical level. We recommend immediate operation irrespective of the condition of the patient, because we feel that the control of hemorrhage is a most important factor in the treatment of coexisting and continuing shock. Hamilton and Duncan also take this view. Antishock measures should be continued along with surgical intervention. Wangensteen suction for decompression is used routinely in all abdominal operations and the tube is passed immediately after the patient has arrived at the hospital. Sulfanilamide, 10 Gm., is placed in the peritoneal cavity in all cases of peritoneal soiling. In spite of the encouraging reports from other clinics, we have not seen any appreciable decrease in the number of cases of peritonitis since we began the use of sulfanilamide intraperitoneally. In twenty-seven cases in which sulfanilamide powder was placed in the peritoneal cavity and sulfonamides were used systemically after operation, eight patients lived and nineteen died, which gives a mortality of 70.4 per cent. Therefore, in our hands, at least, the use of sulfonamides has not appreciably lowered the mortality. In spite of the poor showing made by the use of sulfonamides in our hands, it does

TABLE XV. THORACIC-ABDOMINAL WOUNDS: TWELVE FATAL CASES

CASE NO.	SEX AGE	ENTRANCE WOUNDS OF ABDOMEN	ENTRANCE WOUNDS OF CHEST	OPERATIVE FINDINGS	PNEUMOTHORAX	TIME BEFORE DEATH
1	M 16	Right lower quadrant	4th right interspace anterior axillary line; subcutaneous emphysema	--	--	45 min. after admission; no operation
2	M 35	Right lower quadrant; right costal margin in right upper quadrant	4th right intercostal space	--	--	30 min. after admission; no operation
3	M 35	Right lower quadrant	4th interspace midclavicular line (right arm middle upper third)	--	--	10 min. after admission; no operation
4	M 15	--	2nd right interspace anterior axillary line (lateral aspect right arm)	Perforation of right diaphragm, dome of right liver, left kidney	Minus 3, plus 4, right side	3rd postoperative day
5	M 27	--	8th interspace posteriorly in midscapular line; subcutaneous emphysema	Perforation of stomach and diaphragm	--	1st postoperative day
6	M 29	--	Right intercostal space mid-axillary line	Perforation of right lobe of liver and diaphragm	Underwater drainage	1st postoperative day
7	M 21	--	Left 8th intercostal space anterior axillary line; subcutaneous emphysema	2 penetrations of fundus of stomach	Tension pneumothorax; underwater drainage	2 hr. after operation
8	M 35	--	7th left intercostal space anterior axillary line; subcutaneous emphysema	Perforation of diaphragm and anterior and posterior walls of stomach	Tension pneumothorax	1st postoperative day
9	F 23	--	3rd right intercostal space midclavicular line (gunshot wound in right temporal region of skull)	4 perforations of ileum and of the cecum	--	1st postoperative day
10	M 47	--	Left side of chest at level of 6th dorsal vertebra (neck, left supraclavicular region)	2 perforations of jejunum	--	40th postoperative day
11	F 30	Left upper quadrant; right upper quadrant	Left postaxillary line level of 8th rib	4 perforations of jejunum and 2 of stomach	--	1st postoperative day
12	M 22	--	Jagged bullet wound beneath angle of right scapula at level of 7th dorsal vertebra	8 perforations of small intestine, 2 of stomach, 1 of gall bladder	--	1st postoperative day
13	M 19	--	Anterior axillary line near nipple	Laceration of spleen and dome of diaphragm	--	2nd postoperative day
14	M 65	--	3 penetrating wounds of chest at right anterior axillary line at level of 8th rib, exit at 2nd rib; another bullet wound at level of 3rd right intercostal space	Laceration of liver and perforation of diaphragm	Plus 10, plus 2; underwater drainage	1st postoperative day

not mean that we do not favor their use, because we feel that in a larger number of cases they will help prevent peritonitis. On the other hand, the use of sulfonamides certainly cannot, and never will, take the place of good surgery.

We have used penicillin in five cases in this series, but it is too early for us to draw any conclusions from its use. We do feel that it will help in certain cases and we advise its use postoperatively.

Perforations of hollow viscera were usually repaired by means of purse-string sutures or interrupted Lembert sutures. Injuries to the liver were packed or sutured if there was active bleeding. Injuries to blood vessels were treated by ligating the bleeding vessel. Injuries to the spleen were treated by splenectomy. In this group of cases, operations, other than suturing of perforations of the gastrointestinal tract and diaphragm, were performed, as shown in Table XVI.

TABLE XVI. OPERATIONS OTHER THAN SUTURING OF INTESTINES AND DIAPHRAGM

OPERATION	NUMBER OF CASES
Splenectomy	6
Exteriorized intestine	3
Suprapubic cystostomy	3
Resection of small intestine with side-to-side anastomosis	3
Nephrectomy	1
Removal of coccyx and lower part of sacrum	1
Cecostomy	1
Resection of small intestine with anastomosis over a Murphy button	1
Cholecystectomy	1

There were three patients with laceration of the spleen in which splenectomy was done and all survived. There were three patients with laceration of the spleen and associated injuries in which splenectomy was performed and all three died. In three cases in the series the intestines were exteriorized—the small intestine in two cases and the large intestine in one. The patient with the large intestine exteriorized had four through-and-through perforations of the transverse colon and died on the third postoperative day. In the cases of perforation of the small intestine in which the intestines were exteriorized, one patient lived and one died; they both had multiple through-and-through perforations of the small intestine. The three patients on whom a suprapubic cystostomy operation was performed lived. In three cases resection of the small intestine was done because of multiple through-and-through perforations and these three patients died. In one case a Murphy button was used for anastomosis and the patient died. It has been our experience that resection of the small intestine is a procedure fraught with a high mortality. Suture of the individual perforations is the procedure of choice and we have never seen intestinal obstruction occur as a result of suture of multiple perforations of the intestines. Obviously, if a large blood vessel of the mesentery is injured, the surgeon has no choice and should resect the affected segment of bowel. Under such circumstances, the Murphy button should be used because of the rapidity with which the anastomosis can be made.

In one patient with laceration of the kidney, a nephrectomy was performed and the patient died on the twelfth postoperative day.

Postoperatively all patients should receive blood transfusions and intravenous fluids to combat postoperative shock, correct electrolyte imbalance, and overcome dehydration. The use of sulfonamides and penicillin is recommended in all cases where there has been perforation of a viscus, excepting the spleen.

In most cases in this series drainage was carried out when there was spillage in the peritoneal cavity. Our staff is still divided as to the advantage and necessity of drainage. It is our feeling that a small Penrose drain does no harm and does not add to the mortality, but, in fact, may prevent an occasional death from peritonitis. Drainage does not, however, take the place of careful toilet of the peritoneal cavity at the time of operation or of gentle handling of tissues commensurate with the necessary speed that is indicated in these operations.

SUMMARY

Despite the increasing number of excellent clinical reports of large groups of cases, we have attempted to emphasize certain facts which we felt needed to be constantly brought to the attention of surgeons who are engaged in this work.

1. The presence of abdominal rigidity and tenderness is the most valuable clinical sign of penetrating wounds of the abdomen.

2. A positive abdominal tap or the finding of a pneumoperitoneum on radiographic examination is a valuable diagnostic sign of abdominal penetration in some cases.

3. Immediate operation is indicated in all penetrating wounds of the abdomen; shock is no contraindication. The surgeon should be alert to reduce to a minimum the time between the admission of the patient to the hospital and operation.

4. Blood transfusions and intravenous fluids should be used to reduce shock and effect the necessary fluid balance; this is an immediate and urgent part of the treatment on admission.

5. The surgeon should use sufficiently large incisions to give adequate exposure because a substantially large reducible factor in mortality is caused by missed lesions.

6. Sulfonamides do not take the place of good surgery, but they should be used because we consider them potentially valuable adjuvants. Penicillin should be used postoperatively in cases where there has been a perforation of the gastrointestinal tract.

7. Extreme shock is often indicative of blood vessel injury. Early death upon arrival in the hospital is usually due to an injury of a large blood vessel.

8. "Liver deaths" explain some deaths where there is liver injury that is not primarily due to shock and hemorrhage.

9. Too few papers on this subject detail the post-mortem findings in the fatal cases.

10. Age and physical condition of the patient at the time of injury and the presence or absence of associated injuries are definite factors affecting mortality.

In conclusion, there is no group of wounds which requires more early, energetic teamwork and cooperation on the part of the entire hospital staff and nursing service than gunshot wounds of the abdomen, and a recognition of this fact will be an appreciable factor in the reduction of mortality from such injuries.

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ACUTE PULMONARY EDEMA ASSOCIATED WITH MEDIASTINAL EMPHYSEMA

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MEDIASTINAL emphysema has become recognized as a rather common condition with important clinical aspects. The methods of production are now well understood as a result of experimental studies. Emphysema of the mediastinum has been observed in the following circumstances: as a preoperative and postoperative complication of tracheotomies;[1-4] as a result of blunt trauma to the chest wall, frequently associated with, but not due to, fractured ribs;[5] as a spontaneous occurrence;[6-12] during parturition;[14] during an acute asthmatic attack;[15] as a complication of penetrating wounds of the trachea or bronchus; as a complication of intratracheal anesthesia;[16] after the induction of artificial pneumothorax;[6] as a complication of foreign bodies in the bronchi;[13] and in the presence of unrelieved respiratory obstruction.[2, 13]

CAUSES OF MEDIASTINAL EMPHYSEMA

The experimental work of Macklin and Fischer[13, 17, 18] has done much to clarify the pathogenesis. As a result of overinflation of the pulmonary alveoli, air ruptures into the interstitial tissue of the lung and dissects within the sheaths of the pulmonary vessels to the mediastinum. This is the mechanism of production in those conditions which produce increased intra-alveolar pressure. Thus, it is the mechanism in laryngeal obstruction, foreign bodies in the bronchi with extrusion efforts, during an asthmatic attack, during expulsion efforts in labor, as a result of overinflation during intratracheal anesthesia, in the spontaneous variety, and as a result of blunt trauma to the chest wall.

Some cases of spontaneous mediastinal emphysema develop immediately after severe coughing. Others occur in newborn infants who may have some degree of respiratory obstruction or a compensatory dilatation of the alveoli because of an atelectasis. However, in some cases no cause of alveolar rupture is discernible.[6-12] An aid in the diagnosis of mediastinal emphysema is the presence of loud crepitant râles heard over the precordium which are synchronous with each heartbeat. Hamman[6] described it as a "peculiar crunching, crackling, bubbling sound heard over the heart with each contraction." The sound is sometimes heard only with the patient in certain positions. The presence of subcutaneous crepitation confirms the diagnosis.

Mediastinal emphysema occurring after induction of artificial pneumothorax is probably due to injection of air into the interstitial tissue of the lung through a pleural adhesion.[6]

A common method of production of mediastinal emphysema, which may not involve pulmonary overflation, occurs during tracheotomies performed to

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relieve obstruction of the upper respiratory passages. After the deep facial planes of the neck have been entered and before the trachea has been opened, the extreme inspiratory efforts suck air into the mediastinum from the exterior through the operative incision.

The third mechanism of production is less common. Traumatic perforations of the trachea or bronchus may permit the escape of air into the deep fascial planes and produce a massive mediastinal emphysema.

EFFECTS OF MEDIASTINAL EMPHYSEMA

It is now well established that when sufficient intramediastinal tension develops, air ruptures through the mediastinal pleura into the pleural cavity, producing a pneumothorax.[19] A review of the cases in Roper Hospital in a five-year period reveals three such instances. Numerous cases have been reported.[3, 4, 18] Neffson[1] found seventeen instances in 126 tracheotomies. Injury to the pleura during a tracheotomy frequently has been blamed, but the reported cases reviewed at autopsy have revealed that the pleural domes were intact, indicating that the intrapleural air extended from the mediastinum.

A serious complication of mediastinal emphysema is interference with the circulation in the pulmonary vessels and the consequent development of acute pulmonary edema. Air under pressure in the mediastinum surrounds and obstructs the vessels, obstruction of the pulmonary veins occurring before obstruction of the pulmonary arteries. More blood is forced into the lung than can escape, and the pressure within the pulmonary capillaries rapidly rises. Transudation of fluid from the capillaries occurs and acute pulmonary edema results. The possibility of circulatory failure has been mentioned in the literature[8, 18, 19] but no clear-cut cases of acute pulmonary edema have been reported.

CASE REPORT

A 28-year-old Negro man was admitted to Roper Hospital (Case 26186) Jan. 30, 1944, about forty-five minutes after receiving a stab wound of the neck, inflicted by a "switchblade" knife. Physical examination revealed a well-developed, dyspneic, apprehensive Negro man, complaining of substernal pain and in obviously acute distress. Blood pressure was 120/70, pulse rapid but of good volume. There was a penetrating wound of the neck, about 1 cm. in length, situated just to the left of the midline at the level of the first or second tracheal ring. Both air and blood bubbled back and forth through the wound with each respiration and it was obvious that the trachea had been penetrated by the knife. The neck was distended and palpation revealed the characteristic crepitation of subcutaneous emphysema. Further palpation demonstrated subcutaneous air in the region of both shoulders, the face, upper eyelids, forehead, and superior portion of the thorax. Because of the interference with auscultation by the loud crepitation over the chest, interpretation of the physical signs of the cardiopulmonary examination was difficult; it was thought, however, that left hemopneumothorax was present and that some pneumothorax had occurred on the right side. Radiographic examination of the chest revealed evidence of extensive emphysema of the mediastinum and the soft tissues of the neck, back, shoulders, and lateral chest walls. The remainder of the examination was noncontributory.

Shortly after admission, the administration of oxygen by nasal catheter was begun. It was noted that the emphysema was spreading rapidly. Coincidentally, the patient became more dyspneic and his blood pressure was falling. Accordingly, one hour after admission, a tracheotomy was done at the level of the second tracheal ring under local anesthesia. On

return from the operating room, the patient was breathing more easily but the pulse was rapid and weak and the blood pressure was 100/60. Continued fall in blood pressure was interpreted as shock and, consequently, 500 c.c. of plasma with 500 c.c. of normal saline solution were administered intravenously. Almost immediately after completion of the intravenous infusion, the patient's respiration became labored and irregular and, in spite of continuous oxygen and cardiorespiratory stimulation by metrazol, coramine, and caffeine, he died three hours after operation.

Examination of the body at autopsy revealed that the trachea had been penetrated through both its anterior and posterior walls. Subcutaneous and mediastinal emphysema was pronounced, the latter extending from the root of the neck to the diaphragm. Each pleural cavity contained a small amount of air and about 450 c.c. of clear straw-colored fluid; no blood was noted. Both lungs were boggy and permitted the escape of much frothy material on pressure. Careful examination failed to reveal any evidence of perforation of the apical pleura on either side. There were no other findings of significance. The necropsy diagnosis was penetrating wound of trachea, bilateral hydropneumothorax, subcutaneous emphysema, and acute pulmonary edema.

Comment.—This case represents an example of acute pulmonary edema produced by compression of the pulmonary veins in the mediastinum incident to the massive accumulation of air. It is noted that death occurred after the further production of mediastinal emphysema had been halted by the tracheotomy. The fatal outcome was certainly influenced by the administration of intravenous fluids which raised the pressure in the already overloaded pulmonary capillaries. In retrospect, withdrawal of several hundred cubic centimeters of blood would have been more rational than the intravenous administration of plasma and saline solution.

A small amount of air was found in each pleural cavity at autopsy. Careful dissection of the pleural domes failed to reveal any evidence of injury, indicating that air progressed from the mediastinum to the pleural cavity to produce the pneumothorax. The volume of pneumothorax was small, however, and probably did not greatly influence the course.

CLINICAL IMPLICATIONS

Numerous points of clinical significance may be derived from a review of the causes and effects of mediastinal emphysema. Conditions producing markedly increased intra-alveolar pressure should be avoided or relieved as soon as possible. The often heard plea for early tracheotomies when laryngeal obstruction is progressing is re-emphasized. Preliminary insertion of a bronchoscope into the trachea is indicated in many cases of inflammatory laryngeal obstruction. The tracheotomy may then be done with the bronchoscope in place as an airway. Free communication with additional fascial planes of the neck by dissecting away the investing fascia of the trachea during the tracheotomy should be avoided. The trachea should be opened as soon as possible after the deep fascial planes are entered, in a patient who has laryngeal obstruction.

Intravenous fluids should be omitted in the presence of unrelieved respiratory obstruction, and in any patient who has mediastinal emphysema. If the latter condition produces a dangerous degree of tension, it should be decompressed by a low transverse cervical incision, the mediastinum then being entered by blunt dissection.[5]

A careful examination for pneumothorax should be carried out in all situations in which mediastinal emphysema occurs, particularly after tracheotomies for laryngeal obstruction. Air should be aspirated if it is producing respiratory embarrassment. If tension pneumothorax develops, provision must be made for the continuous escape of air from the pleural cavity by closed decompression.

SUMMARY

The causes and effects of mediastinal emphysema are reviewed. An additional effect, acute pulmonary edema, is discussed and a case presented.

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Editorial

Venous Interruption in Thrombo-Embolic Disease

INTERRUPTION of the femoral veins at the groin, since it was first described by Homans in 1934, has become an accepted method to prevent fatal pulmonary embolism. Unfortunately, but not unexpectedly, as with any new method of treatment, serious complications from the operation are being reported in the literature. The chief one is that instances of interference with the circulation of the extremity occur following the operation. An analysis of these reveals that too much of the venous return from the leg had been interrupted. In some cases not only the common femoral vein but also the saphenous had been interrupted and in some instances a block excision had been done of the femoral vein including the saphenofemoral junction and the proximal ends of the superficial and deep femoral veins. In view of these cases it seems worth while to draw attention to the fact that femoral vein interruptions have been carried out in over 1,000 patients at the Massachusetts General Hospital without a single instance of serious interference with the circulation of the extremity, and the mortality rate from the procedure has been zero. It is felt that this is because we adhere to certain basic principles, and in order to help prevent further catastrophies it seems worth while to innumerate them.

The chief indications for bilateral femoral vein interruption are (1) the presence of venous thrombosis in the deep veins of the lower extremity, (2) the occurrence of a nonfatal pulmonary embolus irrespective of whether or not the legs show signs of venous thrombosis, (3) a concomitant rise in temperature, pulse, and respiration postoperatively in a patient that cannot be explained by some other cause, (4) venous thrombosis diagnosed in one extremity, even though no signs of venous thrombosis are detected in the other, and (5) as a prophylactic measure in patients over 50 years of age who are subjected to major abdominal or pelvic operations for malignant disease. This may be performed as a separate operation or at the same time as the major operative procedure. Prophylactic interruption has also been carried out with good results in elderly patients with fractures of the hip. It is especially valuable in patients with an intratrochanteric type of fracture because of the high incidence of fatal pulmonary embolism in this group.

The purpose of the operation is to interrupt the long column of blood in the femoral and popliteal veins, so that if a clot forms in them it cannot be swept upward to lodge in the pulmonary artery. Interruption of the superficial femoral vein just distal to its junction with the deep femoral may be carried out without danger to the circulation of the extremity in any patient irrespective of his age. It is the safest level for the average surgeon to interrupt this large venous system, since the vessel at this point is free of any tributaries. At the

same time the long venous channel of the legs is interrupted at a sufficiently high level to prevent fatal embolism. The vein may be tied in continuity, but division of it and ligation of each end with a primary ligature and a secondary stitch ligature distal to it in each stump is considered the better procedure. These ligatures should be of the nonabsorbable type, either silk or cotton. The safest method of anesthesia in the postoperative or very ill patient is local infiltration of 1 per cent procaine solution.

Minor pulmonary emboli following femoral vein interruption have occurred in about 5 per cent of our cases. The majority of these probably arise from the profunda femoris branch or the common femoral vein above the point of interruption. Only two deaths from pulmonary embolism have occurred following bilateral femoral vein interruption in our series of 1,000 patients. The superficial femoral veins had been interrupted in one and the common femorals in the other. Neither patient died of a sudden massive embolus, but succumbed to the cumulative effects of relatively small emboli arising from clots in the iliac veins which were superimposed on the ones occurring prior to the vein interruptions.

In some cases, to prevent these postinterruption emboli it is considered a better operation to interrupt the common femoral vein proximal to the profunda branch. In general, this type of interruption should be reserved for those patients in whom a thrombus is found in the common femoral vein, since a secondary thrombus is more apt to form after removal of the primary one than if none was present, and later be dislodged by back pressure in the profunda femoris vein. The surgical interruption of the common femoral vein, if it contains a thrombus, will not endanger the circulation of the extremity, since it already has been occluded. The common femoral vein is relatively short and several large tributaries drain into it, so that it is a more difficult procedure to interrupt it than the superficial femoral vein. One or two of these branches usually must be ligated and divided separately to give sufficient length of vein to permit its safe division and ligation. The division should be distal to the saphenofemoral junction, leaving the saphenous vein as a collateral channel for the venous return. Under no circumstances should the common femoral and the saphenous vein both be interrupted, unless it is found that they are already occluded with thrombi. This is especially true in elderly patients with deficient arterial circulation, since apparently they have as poor a venous collateral as they do an arterial one. A good rule is that unless the dorsalis pedis and posterior tibial arteries can be palpated in the feet, the superficial femoral vein should be interrupted and not the common femoral, unless the latter is already occluded by a thrombus.

Pain and swelling of the leg secondary to thrombophlebitis do not always subside following femoral vein interruption and in a few instances they become more marked due to a spread of the thrombosis distal to the site of vein interruption. In these patients, as an adjunct in treatment, marked amelioration of the pain and swelling can be obtained by paravertebral procaine injection of the lumbar sympathetic chain, as has been recommended by Ochsner.

Interruption of the venous system at a higher level, namely, the inferior vena cava or the common iliac veins, should not be done routinely but reserved

for the unusual case of thrombo-embolic disease, in which the femoral veins have been thrombosed for one week or more and pulmonary emboli are still occurring. This is because the thrombi at this stage of the disease are so adherent that it is impossible to remove them through the femoral veins. Inferior vena cava interruption is also indicated in patients who are having septic pulmonary emboli from sepsis in the pelvis or lower extremities. This is preferable to bilateral common iliac vein interruptions, because the venous systems from both extremities can be interrupted through a single exposure. It should be remembered that it is a major surgical procedure requiring general or spinal anesthesia in contradistinction to femoral vein interruption. The development of postphlebitic lower leg ulcerations and varices of the abdominal wall following inferior vena cava interruption are additional reasons that the operation should not be used routinely in the treatment of thrombo-embolic disease. In a group of twelve caval interruptions in the clinic at Massachusetts General Hospital, two patients have developed indolent ulcers of the lower leg and a third patient has had bilateral recurrence of them, whereas only one transient postphlebitic ulcer has occurred in the group of 1,000 patients with femoral vein interruption.

It is our opinion that if these general principles of venous interruption in the treatment of thrombo-embolic disease are followed, lives will be saved from fatal pulmonary embolism and serious complications will be eliminated. Furthermore, this procedure eliminates the long convalescence necessary in the conservative treatment of thrombophlebitis.

Finally, it should be pointed out that the interruption of these large veins should not be entered into too lightly by the average surgeon unaccustomed to dealing with large blood vessels. Alarming hemorrhage may occur if the femoral vein or one of its tributaries is accidentally torn and the femoral artery may be irreparably damaged in attempting to control it.

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